Physician's Manual

VNS Therapy™ Pulse
Model 102 Generator

and

VNS Therapy™ Pulse Duo
Model 102R Generator

May 2003

Caution: U.S. federal law restricts this device to sale by or on the order of a physician.

VNS THERAPY™ VAGUS NERVE STIMULATION

REF 26-0005-1000/3

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1. BRIEF DEVICE DESCRIPTION

The Cyberonics® VNS Therapy? System, used for vagus nerve stimulation (VNS?), consists of the implantable VNS Therapy Generator, a Lead, and the external programming system used to change stimulation settings[1]. The Pulse Generator is an implantable, multiprogrammable, pulse generator that delivers electrical signals to the vagus nerve. The Pulse Generator is housed in a hermetically sealed titanium case and is powered by a single battery. Electrical signals are transmitted from the Pulse Generator to the vagus nerve by the Lead. The Lead and the Pulse Generator make up the implantable portion of the VNS Therapy System.

The external programming system includes the Model 201 Programming Wand, the Model 250 Software, and a compatible computer. (See the Model 250 Physician's Manual for a list of compatible computers.) The Software allows a physician to place the Programming Wand over the Pulse Generator to read and change device settings.

[1] Cyberonics is a registered trademark of Cyberonics, Inc. The VNS Therapy Pulse Generator is protected under U.S. Patent Nos. 4,702,254; 4,867,164; 5,025,807; 5,154,172; 5,186,170; 5,179,950; and 5,235,980. The Read Only Memory (ROM) code has also been copyrighted. The company also holds patents in foreign countries.

1.1. VNS Therapy System Compatibility

The VNS Therapy Pulse, Model 102 Generator, and the VNS Therapy Pulse Duo, Model 102R Generator, are compatible with different Lead types as follows:

? ? **Model 102 Generator:**

Compatible with Model 302 Lead

? ? **Model 102R Generator:**

Compatible with Model 300 Lead (dual pin)

Except for Leads, both Models 102 and 102R are compatible with the following system components:

		Pulse Generator Model	
Component	**Model**	102	102R
Lead	300		**x**
	302	**x**	
Wand	200	**x**	**x**
	201	**x**	**x**
Software	250 v.4.6, 6.1, or higher	**x**	**x**
Tunneler	402	**x**	**x**
Accessory Pack	502	**x**	**x**
Magnets	220	**x**	**x**

1.2. Symbols and Definitions

Symbols and definitions used in this manual include the following:

 Notice for reader to pay special attention to the following details

SN Serial Number

 Expiration Date (Use-Before Date)

 Single Use Only / Do Not Reuse

 Date of Manufacture (Date Product is Labeled)

Contents Sterilized by Ethylene Oxide

 Storage Temperature

2. INTENDED USE / INDICATIONS

The VNS Therapy System is indicated for use as an adjunctive therapy in reducing the frequency of seizures in adults and adolescents over 12 years of age with partial onset seizures that are refractory to antiepileptic medications.

3. CONTRAINDICATIONS

⚠ The VNS Therapy System cannot be used in patients after a bilateral or left cervical vagotomy.

⚠ Do not use shortwave diathermy, microwave diathermy or therapeutic ultrasound diathermy (hereafter referred to as diathermy) on patients implanted with a VNS Therapy System. Diagnostic ultrasound is not included in this contraindication.

Energy delivered by diathermy may be concentrated into or reflected by implanted products such as the VNS Therapy System. This concentration or reflection of energy may cause heating.

Testing indicates that diathermy can cause heating of the VNS Therapy System well above temperatures required for tissue destruction. The heating of the VNS Therapy System resulting from diathermy can cause temporary or permanent nerve or tissue or vascular damage. This damage may result in pain or discomfort, loss of vocal cord function, or even possibly death if there is damage to blood vessels.

Because diathermy can concentrate or reflect its energy off any size-implanted object, the hazard of heating is possible when any portion of the VNS Therapy System remains implanted, including just a small portion of the Lead or electrode. Injury or damage can occur during diathermy treatment whether the VNS Therapy System is turned “on” or “off”.

Diathermy is further prohibited because it may also damage the VNS Therapy System components resulting in loss of therapy, requiring additional surgery for system explantation and replacement. All risks associated with surgery or loss of therapy (loss of seizure control) would then be applicable.

Advise your patients to inform all their health care professionals that they should not be exposed to diathermy treatment.

4. WARNING

Physicians should inform patients about all potential risks and adverse events discussed in the VNS Therapy System physician's manuals.

⚠ The **safety and efficacy** of the VNS Therapy System has not been established for uses not covered in the "Intended Use/ Indications" section of this manual.

⚠ The safety and efficacy of the VNS Therapy System treatment have not been established for stimulation of the **right vagus nerve** or of any other nerve, muscle, or tissue.

⚠ **Excessive stimulation** at an excess duty cycle (that is, one that occurs when ON time is greater than OFF time) has resulted in degenerative nerve damage in laboratory animals. An excess duty cycle can be produced by continuous or frequent magnet activation (? 8 hours), as determined by animal studies. Cyberonics recommends against stimulation at these combinations of ranges.

⚠ **Aspiration** may result from the increased swallowing difficulties reported by some patients during stimulation. Patients who have **pre-existing swallowing difficulties** are at greater risk for aspiration.

⚠ **Device malfunction** could cause painful stimulation or direct current stimulation. Either event could cause nerve damage and other associated problems. Patients should be instructed to use the magnet to stop stimulation if they suspect a malfunction, and then to contact their physician immediately for further evaluation. Prompt surgical intervention may be required if a malfunction occurs.

⚠ Susceptible patients with predisposed dysfunction of cardiac conduction systems (re-entry pathway) have not been studied as part of controlled clinical trials to establish the safety of VNS Therapy System treatment in these patients. Evaluation by a cardiologist is recommended if the family history, patient history, or electrocardiogram suggests an abnormal cardiac conduction pathway. Serum electrolytes, magnesium, and calcium should be documented before implantation. Post-implant electrocardiograms and Holter monitoring are recommended if clinically indicated.

⚠ **Sudden unexplained death in epilepsy (SUDEP):** Through August 1996, 10 sudden and unexplained deaths (definite, probable, and possible) were recorded among the 1,000 patients implanted and treated with the VNS Therapy device. During this period, these patients had accumulated 2,017 patient-years of exposure.

Some of these deaths could represent seizure-related deaths in which the seizure was not observed, at night, for example. This number represents an incidence of 5.0 definite, probable, and possible SUDEP deaths per 1,000 patient-years.

Although this rate exceeds that expected in a healthy (nonepileptic) population matched for age and sex, it is within the range of estimates for epilepsy patients not receiving vagus nerve stimulation, ranging from 1.3 SUDEP deaths for the general population of patients with epilepsy, to 3.5 (for definite and probable) for a recently studied antiepileptic drug (AED) clinical trial population similar to the VNS Therapy System clinical cohort, to 9.3 for patients with partial onset epilepsy.

⚠ Patients with obstructive sleep apnea (OSA) may have an increase in apneic events during stimulation. Cyberonics recommends care when treating patients with preexisting OSA. Lowering stimulus frequency or prolonging OFF time may prevent exacerbation of OSA.

⚠ **The VNS Therapy device is not curative:** Physicians should warn patients that the VNS Therapy System is not a cure for epilepsy and that since seizures may occur unexpectedly, patients should consult with a physician before engaging in unsupervised activities, such as driving, swimming, and bathing, and in strenuous sports that could harm them or others.

5. PRECAUTIONS

Physicians should inform patients about all potential risks and adverse events discussed in the VNS Therapy System Physician's Manuals.

⚠ **Laryngeal irritation** may result from stimulation. **Patients who smoke** may have an increased risk of laryngeal irritation.

⚠ **Dyspnea** may result from stimulation. **Patients with chronic obstructive pulmonary disease** may have an increased risk of dyspnea.

⚠ It is important to follow **recommended implantation procedures and intraoperative product testing** described in this manual. During the intraoperative Lead Test, rare incidents of bradycardia and/or asystole have occurred. As of October 1998, approximately 3,000 patients had been implanted with the VNS Therapy System. Four of these patients were reported to have experienced **bradycardia and/or asystole** during the intraoperative Lead Test. All four patients recovered without sequelae. One of the four patients was implanted with the VNS Therapy System. There were no postoperative or VNS Therapy treatment-related cardiac adverse events later reported for that patient. No similar events were reported to have occurred during the clinical studies at the time of implantation or during treatment.

The safety of this therapy has not been systematically established for patients experiencing bradycardia or asystole during VNS Therapy System implantation.

⚠ **Reversal of Lead polarity has been associated with an increased chance of bradycardia** in animal studies. It is important to make sure that the Lead connector pins are correctly inserted (white marker band/serial number to + connection) into the Lead receptacle(s).

⚠ **Do not program the VNS Therapy System to an ON or periodic stimulation treatment for at least 14 days after the initial or replacement implantation.** Failure to observe this precaution may result in patient discomfort or adverse events.

⚠ **Resetting the Pulse Generator** turns the device OFF (output current = 0 mA), and all device history information is lost. The device history information should be printed out before resetting.

⚠ **Do not use frequencies of 5 Hz or below for long-term stimulation.** Because these frequencies generate an electromagnetic trigger signal, their use results in excessive battery depletion of the implanted Pulse Generator and, therefore, should be used for short periods of time only.

⚠ It is important to follow **infection control procedures**. Infections related to any implanted device are difficult to treat and may require that the device be explanted. Cyberonics recommends that the patient be given antibiotics preoperatively. The surgeon should ensure that all instruments are sterile prior to the operation.

Cyberonics recommends frequent irrigation of both incision sites with generous amounts of bacitracin or equivalent solution prior to closure. (To minimize scarring, these incisions should be closed with cosmetic closure techniques.) Also, antibiotics should be administered postoperatively at the discretion of the physician.

⚠ The VNS Therapy System is indicated for use only in stimulating the **left vagus nerve** in the neck area inside the carotid sheath.

⚠ The VNS Therapy System is indicated for use only in stimulating the **left vagus nerve below where the superior and inferior cervical cardiac branches separate from the vagus nerve.**

⚠ **Physicians who implant the VNS Therapy System** should be experienced performing surgery in the carotid sheath; physicians should be familiar with vagal anatomy, particularly the cardiac branches; and they should be trained in the surgical technique relating to implantation of the VNS Therapy System. See the section “Physician Training/Information” in this manual.

⚠ A **neck brace** can be used by the patient for the first week to help ensure proper Lead stabilization.

⚠ **Appropriate physician training** is very important:

- ✍✍ **Prescribing physicians** should be experienced in the diagnosis and treatment of epilepsy and should be familiar with the programming and use of the VNS Therapy System.
- ✍✍ **Physicians who implant the VNS Therapy System** should be experienced performing surgery in the carotid sheath and should be trained in the surgical technique relating to implantation of the VNS Therapy System. (See the "Physician Training/Information" section of this manual for more information.)

5.1. Sterilization, Storage, and Handling

The Pulse Generator and accessories have been sterilized using ethylene oxide gas (EO) and are supplied in a sterile package to permit introduction into the operating field. A process indicator is included in the package; devices should be implanted only if the indicator is green. An expiration (or use-before) date is marked on each package.

The implantable portions of the VNS Therapy System are nonpyrogenic.

⚠ **Store the Pulse Generator** between -20?C (-4?F) and +55?C (+131?F). Temperatures outside this range can damage components.

⚠ **Do not store the Pulse Generator** where it is exposed to water or other liquids. Moisture can damage the seal integrity of the package materials.

⚠ **Do not implant a device** if any of the following has occurred:

- ✍ The device has been dropped, because dropping it could damage Pulse Generator components.
- ✍ The process indicator within the inner package is not green for product sterilized by EO.
- ✍ The storage package has been pierced or altered, because this could have rendered it nonsterile.
- ✍ The expiration (use-before) date has expired, because this can adversely affect the Pulse Generator's longevity and sterility.

⚠ **Do not ultrasonically clean the Pulse Generator**, because doing so may damage Pulse Generator components.

⚠ **Do not re-sterilize the Pulse Generator**. Return any opened devices to Cyberonics.

⚠ The Pulse Generator is a single-use-only device. **Do not reimplant** an explanted Pulse Generator for any reason, because infections may occur.

Explanted generators should be returned to Cyberonics for examination and proper disposal, along with a completed Returned Product Report form. Before returning the Pulse Generator, disinfect the device components with Betadine®, Cidex® soak, or other similar disinfectant, and double-seal them in a pouch or other container properly labeled with a biohazard warning.

⚠ **Do not incinerate the Pulse Generator;** it contains a sealed chemical battery, and an explosion could result.

5.2. Lead Evaluation and Connection

⚠ **Do not use a lead other than** the Model 300 Lead with the Model 102R Generator or a Model 302 Lead with the Model 102 Generator because such use may damage the Pulse Generator or injure the patient.

⚠ Exercise extreme caution if testing the Lead using **line-powered equipment** because leakage current can injure the patient.

⚠ Do not insert a Lead in the Pulse Generator Lead receptacle(s) without first visually **verifying that the setscrew(s) is sufficiently retracted** to allow insertion. Avoid backing the setscrew(s) out further than needed for Lead insertion.

⚠ Ensure that the hex screwdriver is fully inserted in the setscrew, and then push in on the hex screwdriver and turn it clockwise until it clicks. To avoid damaging (stripping) the setscrew(s) and/or dislodging the setscrew plug(s), insert the hex screwdriver into the center of the setscrew plug, keeping it perpendicular to the Pulse Generator.

5.3 Environmental and Medical Therapy Hazards

⚠ Patients should exercise reasonable caution in avoiding devices that generate a **strong electric or magnetic field**. (For examples, see the "Other Environmental Hazards" section of this manual.) If a Pulse Generator ceases operation while in the presence of electromagnetic interference (EMI), moving away from the source may allow it to return to its normal mode of operation.

5.3.1. Hospital and Medical Environments

⚠ VNS Therapy System operation **should always be checked** by performing device diagnostics after any of the procedures mentioned in this manual. Additional precautions for these procedures are described below.

⚠ **For clear imaging, patients may need to be specially positioned for mammography procedures** because of the location of the Pulse Generator in the chest. (Most routine diagnostic procedures, such as fluoroscopy and radiography, are not expected to affect system operation.)

⚠ **Therapeutic radiation** may damage the Pulse Generator's circuitry, although no testing has been done to date and no definite information on radiation effects is available. Sources of such radiation include therapeutic radiation, cobalt machines, and linear accelerators. The radiation effect is cumulative, with the total dosage determining the extent of damage. The effects of exposure to such radiation can range from a temporary disturbance to permanent damage, and may not be detectable immediately.

⚠ **External defibrillation** may damage the Pulse Generator. Attempt to minimize current flowing through the Pulse Generator and Lead system by following these precautions:

- ✍✍ Position defibrillation paddles perpendicular to the Pulse Generator and Lead system and as far from the Pulse Generator as possible.
- ✍✍ Use the lowest clinically appropriate energy output (watt-seconds).
- ✍✍ Confirm Pulse Generator function after any internal or external defibrillation.

⚠ Use of electrosurgery (electrocautery or radio frequency (RF) ablation devices) may damage the Pulse Generator. Attempt to minimize the current flowing through the Pulse Generator and Lead system by following these precautions:

- ✍✍ Position the electrosurgery electrodes as far as possible from the Pulse Generator and Lead.
- ✍✍ Avoid electrode placement that puts the Pulse Generator or Lead in the direct path of current flow or within the part of the body being treated.
- ✍✍ Confirm Pulse Generator functions as programmed after electrosurgery.

⚠ **Magnetic resonance imaging** (MRI) should not be performed with a magnetic resonance body coil in the transmit mode. The heat induced in the Lead by an MRI body scan can cause injury.

If an MRI should be done, use only a transmit and receive type of head coil. Magnetic and RF fields produced by MRI may change the Pulse Generator settings (change to reset parameters) or activate the device. Stimulation has been shown to cause the adverse events reported in the "Adverse Events" section of this manual. MRI compatibility was demonstrated using a 1.5T General Electric Signa Imager with a Model 100 only. The Model 102 and Model 102R are functionally equivalent to the Model 100. Testing on this imager as performed on a **phantom**[2] **indicated that the following Pulse Generator and MRI**

[2] A phantom is a material resembling a body in mass, composition, and dimensions that is used to measure absorption of radiation.

procedures can be used safely without adverse events:

- Pulse Generator output programmed to 0 mA for the MRI procedure, and afterward, retested by performing the Lead Test diagnostics and reprogrammed to the original settings
- Head coil type: transmit and receive only
- Static magnetic field strength: ? 2.0 tesla
- Specific-rate absorption (SAR): ? 1.3 W/kg for a 154.5-lb (70-kg) patient
- Time-varying intensity: ? 10 tesla/sec

Use caution when other MRI systems are used, since adverse events may occur because of different magnetic field distributions.

⚠ Procedures in which the RF is transmitted by a body coil should not be done on a patient who has the VNS Therapy System. Thus, protocols must not be used that utilize local coils that are RF-receive only, with RF-transmit performed by the body coil. Note that some RF head coils are receive-only, and that most other local coils, such as knee and spinal coils, are also RF receive-only. **These coils must not be used in patients with the VNS Therapy System.**

⚠ **Extracorporeal shockwave lithotripsy** may damage the Pulse Generator. If therapeutic ultrasound therapy is required, avoid positioning the Pulse Generator part of the body in the water bath or in any other position that would expose it to ultrasound therapy. If that positioning cannot be avoided, program the Pulse Generator output to 0 mA for the treatment, and then after therapy, reprogram the Pulse Generator to the original parameters.

⚠ If the patient receives medical treatment for which electric current is passed through the body (such as from a TENS unit) either the Pulse Generator output should be set to 0 mA or function of the Pulse Generator should be monitored during initial stages of treatment.

⚠ **Therapeutic ultrasound.** Routine therapeutic ultrasound could damage the Pulse Generator and may be inadvertently concentrated by the device, causing harm to the patient.

5.3.2. Home Occupational Environments

Properly operating microwave ovens, electrical ignition systems, power transmission lines, theft-prevention devices, and metal detectors are not expected to affect the Pulse Generator. Similarly, most routine diagnostic procedures, such as fluoroscopy and radiography, are not expected to affect system operation. However, because of their higher energy levels, sources such as transmitting antennas may interfere with the VNS Therapy System. It is suggested that the Pulse Generator be moved away from equipment—typically at least six feet (1.8 meters)—that may be causing interference.

⚠ The patient should seek medical advice before entering environments that are protected by a warning notice preventing entry by patients implanted with a cardiac pacemaker or defibrillator.

5.3.3. Cellular Phones

Based on testing to date, cellular phones have no effect on Pulse Generator operation. Unlike an implanted pacemaker or defibrillator, the Pulse Generator does not sense physiologic signals.

5.3.4. Other Environmental Hazards

⚠ Strong magnets, hair clippers, vibrators, loudspeaker magnets, Electronic Article Surveillance (EAS) System tag deactivators, and other similar electrical or electro-mechanical devices, which may have a strong static or pulsing magnetic field, can cause accidental magnet activation. Patients should be cautioned to keep such devices away from the Pulse Generator, typically at least six inches (15 centimeters) away.

5.3.5. Programming Software

The Pulse Generator can be programmed using the Model 250 Software, Version 4.6, Version 6.1, or higher. The Software should be used on a laptop or handheld computer dedicated only to programming the VNS Therapy System. (For more information, see the Model 250 Software Physician's Manual for Version 4.6, Version 6.1, or higher, including a list of computers that have been qualified for use with this Software.)

5.3.6. Pulse Generator and EMI Effects on Other Devices

During stimulation, the Pulse Generator may interfere with devices operating in the 30 kHz to 100 kHz range, such as pocket transistor radios and hearing aids. This interference is a theoretical possibility, and no effects on hearing aids have yet been reported, although the Pulse Generator can interfere with a transistor radio when held directly over one. No specific testing has been done to date, and no definite information on effects is available.

The Pulse Generator should be moved—typically at least six feet (1.8 meters)—away from equipment with which it may be interfering.

Programming or interrogating the Pulse Generator may momentarily interfere with other sensitive electronic equipment nearby. The Pulse Generator is not expected to trigger airport metal detectors or theft-protection devices that are closer than about six feet (1.8 meters).

⚠ The Pulse Generator may affect the operation of **other implanted devices,** such as cardiac pacemakers and implantable defibrillators. Possible effects include sensing problems and inappropriate Pulse Generator responses. If the Pulse Generator patient requires concurrent implantable pacemaker and/or defibrillator therapy, careful programming of each system is necessary to optimize the patient's benefit from each device.

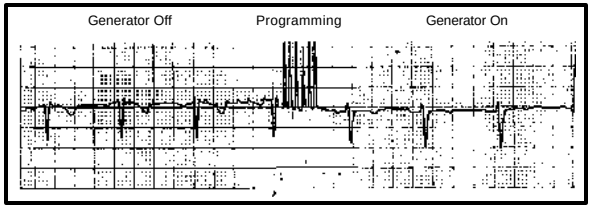
⚠ The magnet provided for activation or inhibition of the Pulse Generator may damage **televisions, computer**

disks, credit cards, and other items affected by strong magnetic fields.

5.3.7. Effects on ECG Monitors

Pulse Generator data communication produces an ECG artifact, an example of which is shown in the ECG tracings in Figure 1:

Figure 1. ECG Artifact Produced by Pulse Generator Communication



5.3.8. Pulse Generator Disposal

⚠ Do not incinerate the Pulse Generator, because it can explode if subjected to incineration or cremation temperatures.

⚠ Return all explanted Pulse Generators to Cyberonics for examination and safe disposal.

⚠ Do not implant an explanted Pulse Generator in another patient, because sterility, functionality, and reliability cannot be ensured.

6. ADVERSE EVENTS

The VNS Therapy System was implanted in 454 patients in five clinical studies involving 611 devices (some patients had Pulse Generator replacements). As of August 1996, total VNS Therapy exposure in these 454 patients was 901 device-years. Individual patient exposure averaged 24 months, with a range of eight days to 7.4 years.

A total of nine patients died during these five studies. One patient died from each of the following: thrombotic thrombocytopenic purpura, drowning, aspiration pneumonia, pneumonia, and renal failure associated with drug and alcohol ingestion. No cause of death was apparent for the other four deaths, which may be classified as sudden unexpected death in epilepsy (SUDEP). None of these deaths were attributed by the investigators to the VNS Therapy System.

6.1. Adverse Events Observed in Studies

Included among the five clinical trials were two randomized, blinded, active control trials (Study E03 and E05), which involved 314 patients and the implantation of 413 devices, yielding a total VNS Therapy System exposure (inclusive of long-term follow up) of 591 device years. These trials form the basis of the rates of observed adverse events. Table 1 contains only a partial list of the more common and expected observed adverse events associated with the VNS Therapy System. A comprehensive listing of adverse events observed in studies is available by study from the Clinical Research department at Cyberonics.

Table 1 reports the adverse events from these studies during the randomized phase (approximately a 14-week observation period) and randomized phase plus long-term follow up (? 3 months) through August 1996. The most common side effect associated with stimulation was hoarseness (voice alteration), which, depending on device settings, can be severe to barely perceptible. Hoarseness is reported to occur primarily during the ON period of stimulation.

Table 1. Observed Adverse Events

N=413 devices in 314 patients,
152 patients in the HIGH treatment group, 591 device years

	Randomized + Long-Term Follow Up (? 3 Months) N=314 Patients, 591 Device-Years				Randomized Phase, HIGH Only, N=152 Pts	
Adverse Event (AE)	**No. of Patients***	**% of Patients†**	**No. of Events**	**Events/ Device-Year**	**No. of Patients**	**% of Patients**
Serious AEs‡						
Surgically related	13	4.1	13	0.022	N/A	N/A
Stimulation related	4	1.2	4	0.007	1	0.7
Non-serious AEs						
Voice alteration	156	50	720	1.228	91	60
Increased coughing	129	41	456	0.772	57	38
Pharyngitis	84	27	182	0.308	36	24
Paresthesia	87	28	377	0.638	32	21
Dyspnea	55	18	55	0.093	32	21
Dyspepsia	36	12	98	0.166	22	15
Nausea	59	19	154	0.261	21	14
Laryngismus	10	3.2	30	0.051	9	5.9

* Number of patients reporting the event at least once.

† Percentage of patients reporting the event at least once.

‡ Included infection, nerve paralysis, hypesthesia, facial paresis, left vocal cord paralysis, left facial paralysis, left hemidiaphragm paralysis, left recurrent laryngeal nerve injury, urinary retention, and low-grade fever.

Status epilepticus: Valid estimates of the incidence of treatment-emergent status epilepticus among VNS Therapy System treated patients are difficult to obtain because Investigators participating in clinical trials did not all employ identical rules for identifying cases. At a minimum, two of 441 adult patients had episodes that could be described unequivocally as "status." In addition, a number of reports were made of variably defined episodes of seizure exacerbation (for example, seizure clusters and seizure flurries).

Rebound after stimulation was stopped: Seizure frequency was monitored for one to four weeks after stimulation was stopped because of battery depletion in 72 instances (68 patients) in Study E03. Of these instances, 11 of the 72 (15%) **had a greater than 25 percent increase above baseline, and 42** of the 72 (58%) had a greater than 25 percent decrease in seizure rate. The seizure rate increased by more than 1.5 standard deviations above baseline in 10 percent of instances (compared with the 7 percent expected).

6.2. Potential Adverse Events

Adverse events reported during clinical studies as statistically significant are listed below in alphabetical order[3]:

- Ataxia (muscle movements or twitching, generally associated with stimulation)
- Dyspepsia (indigestion)
- Dyspnea (difficulty breathing, shortness of breath)
- Hypesthesia (impaired sense of touch)

[3] The lay terms provided correspond to those in the Patient's Manual.

? ? Increased coughing
? ? Infection
? ? Insomnia (inability to sleep)
? ? Laryngismus (throat, larynx spasms)
? ? Nausea
? ? Pain
? ? Paresthesia (prickling of the skin)
? ? Pharyngitis (inflammation of the pharynx, throat)
? ? Voice alteration (hoarseness)
? ? Vomiting

Other potential adverse events possibly associated with surgery or stimulation include, but are not limited to, the following:

? ? Aspiration (fluid in the lungs)
? ? Blood clotting
? ? Choking sensation
? ? Damage to nerves or vasculature in the surgical area, including the carotid artery and jugular vein
? ? Device (Generator and/or Lead) migration or extrusion
? ? Dizziness
? ? Dysphagia (difficulty swallowing)
? ? Duodenal ulcer, gastric ulcer
? ? Ear pain
? ? Facial flushing
? ? Facial paralysis, paresis
? ? Foreign body reaction to implants, including possible tumor formation
? ? Formation of fibrous tissue, pockets of fluid

? ? Heart rate and rhythm changes
? ? Hiccuping
? ? Incision site pain
? ? Irritability
? ? Laryngeal irritation (sore, painful throat)
? ? Left hemidiaphragm paralysis
? ? Left recurrent laryngeal nerve injury
? ? Left vocal cord paralysis
? ? Low-grade fever
? ? Muscle pain
? ? Neck pain
? ? Nerve injury
? ? Painful or irregular stimulation
? ? Skin, tissue reaction
? ? Stomach discomfort
? ? Tinnitus (ringing in the ears)
? ? Tooth pain
? ? Unusual scarring at the incision site
? ? Urinary retention
? ? Vagus nerve paralysis
? ? Weight change
? ? Worsening of asthma and bronchitis

⚠ Patients who manipulate the Pulse Generator and Lead through the skin may damage or disconnect the Lead from the Pulse Generator and/or possibly cause damage to the vagus nerve.

7. CLINICAL STUDIES

Five acute-phase clinical studies involving the VNS Therapy System have been conducted (see Table 2). These studies enrolled 537 patients, of whom 454 were implanted with the VNS Therapy System. A total of 611 devices were implanted, and patient exposure totaled 901 device-years, with an individual mean patient exposure of 24 months (ranging from eight days to 7.4 years). A total of 45 centers participated in these studies: 40 in the United States, 2 in Germany, and 1 each in Canada, Holland, and Sweden.

Table 2. Description of Clinical Studies

All patients enrolled in all clinical studies, N=537

Description of Clinical Studies						
	Longitudinal			Parallel		
Study	**E01**	**E02**	**E04**	**E03**	**E05**	**Total**
Type of study	pilot longitudinal	pilot longitudinal	open longitudinal	randomized parallel high/low	randomized parallel, high/low	-
No. of patients enrolled	11	5	133	126	262	537
No. of centers*	3	2	24	17	20	45
Reference period (baseline)	weeks 2–4	weeks 3–6	weeks -4–0	weeks -12–0	weeks -12–0	-
Seizure type	partial	partial	all types	partial	partial	-
No. of AEDs	1–2	1–2	not specified	0–3	1–3	-

* Total includes non-U.S. centers (Canada, Holland, Germany -2, and Sweden); several U.S. centers participated in more than one study.

Purpose: The purpose of the studies was to determine whether adjunctive use of optimal stimulation of the left vagus nerve could reduce seizure frequency in patients with refractory seizures.

Methods: In the two randomized, blinded, active control trials (E03 and E05), patients were randomly assigned to either of two treatment groups: HIGH (believed to be therapeutic) or LOW (believed to be less therapeutic). Patients enrolled in the study were seen every four weeks during the baseline period (weeks -12 to 0). Patients meeting eligibility were implanted with the Pulse Generator and Lead (see Table 3).

Two weeks after implantation, patients were randomized to the HIGH or LOW stimulation group, and the Pulse Generator was activated. Patients in the HIGH groups received a higher frequency, greater pulse width, and higher duty cycle of stimulation. The randomized treatment period that followed activation of the Pulse Generator lasted 14 weeks (the last 12 weeks of which were used in the efficacy analysis —the first two weeks for a treatment ramp-up period).

Table 3. Description of Patients

All patients implanted in all clinical studies, N=454

Description of Patients						
	Longitudinal			Parallel		
Study	**E01**	**E02**	**E04**	**E03**	**E05**	**Total**
No. of patients implanted	11	5	124	115	199	454
No. of patients stimulated	10	5	123	115	198	451
Age (range)	32 (20–58)	33 (18–42)	24 (3–63)	33 (13–57)	33 (13–60)	32 (3–63)
No. of females (%)	4 (36%)	2 (40%)	57 (46%)	43 (37%)	104 (52%)	210 (46%)
Years with epilepsy (range)	22 (13-32)	20 (5-36)	17 (0.8-48)	21 (4-47)	23 (2-52)	21 (0.8-52)
No. of AEDs (av)	1.0	1.0	2.2	2.1	2.1	2.1
Median no. of seizures per day at baseline	0.6	0.42	0.65	0.70 high/ 0.85 low	0.58 high/ 0.51 low	-

Results: The primary efficacy endpoint (percent reduction in seizure rate) was measured over 12 weeks (see Table 4). Adverse events were assessed at each patient visit.

Table 4. Principal Efficacy and Safety Results

All patients in efficacy analyses in all clinical studies, N=441

Principal Efficacy Results						
	Longitudinal			Parallel		
Study	**E01**	**E02**	**E04**	**E03**	**E05**	**Total**
No. of patients in efficacy analysis	10	5	116	114	196	441
Median reduction in seizures/day	32%*	48%	22%*	23% high*/ 6% low	23% high†/ 21% low†	-
Mean reduction in seizures/day	24%‡	40%	7%‡	24% high‡/ 6% low	28% high†/ 15% low†	-
Difference in mean (high/low)	-	-	-	17%§ (3%/31%)	13%‖ (2%/23%)	-
% with ? 50% response	30%	50%	29%	30% high/ 14% low	23% high/ 16% low	-
Principal Safety Results Through Long-term Follow Up						
Exposure (pt-yr)	45	20	245	456	135	901
SAEs¶ (high/low)	9%/ -	0%/ -	6%/ -	5%/0%	7%/9%	-
Discontinued (LOE/AE) #	0/1	0/0	2/3	0/2	1/3	3/9
No. of explants**	2	2	15	9	5	33
Deaths: SUDEP/total ††	0/0	0/0	3/4	0/3	1/2	4/9

Within group broad analyses:

* P ? 0.05, by Wilcoxon sign rank.

† P < 0.0001, by ANOVA.

‡ P ? 0.05, by Student's *t-test.*

Between group broad analyses:

§ P ? 0.02, by Wilcoxon rank sum; P ? 0.02, by Student's *t-test.*

|| P ? 0.04, by aligned ranks test; P ? 0.02, by Student's *t-test*; P ? 0.03, by ANOVA.

Safety information:

¶ SAEs = serious adverse events.

Discontinuing for lack of efficacy (LOE)/adverse events (AE) at one year, excluding deaths.

** Number of explants through August 1996, excluding deaths.

†† All deaths occurred by the long-term follow-up closing date of August 1996.

⚠ For completeness, Study E04 data—which included patients younger than 12 and those with generalized seizures—are presented in Tables 3 and 4.

Figure 2 and Table 5, which follow, show the results from Study E05, the largest and most recent of the randomized, blinded, active control studies:

Figure 2. Change in Seizure Frequency, Patient Distribution

(With Corresponding Table)

All E05 patients completing effectiveness evaluation, N=196

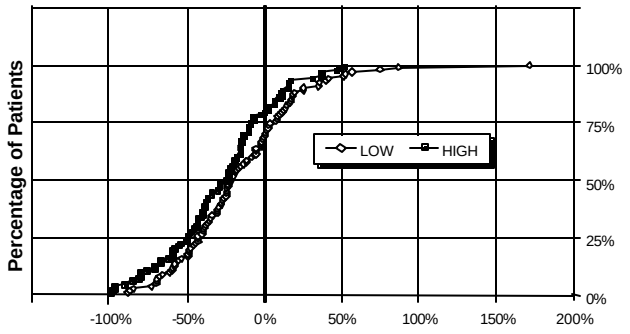


Table 5. Principal Effectiveness Statistics (E05)

All patients in E05 effectiveness analyses, N=196

Percentage Change (Seizures/Day) from Baseline			
Statistics	**High (94)**	**Low (102)**	**Difference**
Median	-23%	-21%	N/A
25%, 75% Quartiles	-8.9%, -49%	4.0%, -43%	N/A
95% Confidence intervals	-35%, -21%	-23%, -7.7%	-23%, -2.3%
Range (min, max)	-100%, 52%	- 89%, 171%	-23%, -2.3%
Mean ? SD	-28% ? 34%	-15% ? 39%	-13%* ? 37%

* Difference is statistically significant (P ? 0.05) by analysis of variance (P=0.032) and by Cochran-Mantel-Haenszel aligned ranks (P=0.040).

Patient response to VNS Therapy was examined using statistical modeling (examining group characteristics) and an evaluation of individual patients. No useful predictors were found of an increase or a decrease in seizure frequency.

Conclusions: Patients with refractory partial onset seizures treated with HIGH VNS Therapy had a statistically significant decrease in frequency of seizures, compared with the baseline and compared with patients treated with LOW (active control) VNS Therapy. As indicated in Figure 2, most patients had a reduction in seizure frequency; some, however, had either no change or an increase in seizure frequency. The most common treatment-related adverse events were voice alteration and dyspnea. Treatment was well tolerated, with 97 percent (306 of 314) of the implanted patients continuing into the long-term follow-up phase of the study.

7.1. Long-Term Data from Uncontrolled Follow Up

Long-term data (? 3 months' stimulation) were collected on all available E01 through E04 study patients (see Table 6). At the time the VNS Therapy System Premarket Approval Application was considered by the U. S. Food and Drug Administration, long-term data on most Study E05 patients were not available. These long-term follow-up data are uncontrolled because they come from an open-label protocol in which both the antiepileptic drug medications and the VNS Therapy device settings were allowed to be changed.

Ninety-five percent (95%) of patients were continuing one year after their original implant; 82 percent were still receiving stimulation at two years; and 69 percent were receiving stimulation at three years. Some E04 patients had not yet had the opportunity to reach two or three years of stimulation and therefore were not used in the calculations. Additionally, 28 E03 patients were implanted outside the United States in countries that later received commercial approval, and data were available through one year of stimulation only.

Table 6. Patient Summary Chart

Patients continuing treatment as of 8/22/96

Study	E01	E02	E03	E04	Total
No. of patients randomized/stimulated	10	5	115	123	253
No. of patients entering long-term phase	10	5	113	123	251
No. of continuing patients being treated for up to 1 year/No. started	10/10	5/5	111/115	112/121*	238/251
No. of continuing patients being treated for up to 2 years/No. started	9/10	4/5	71/87†	58‡/70	142/172
No. of continuing patients being treated for up to 3 years/No. started	7/10	3/5	57/87	21§24	88/126

* Two E04 Study patients had not been implanted long enough to reach the one-year date after implantation.

† Twenty-eight (N=28) commercial European patients were excluded from follow up after one year of treatment due to the commercial release of the VNS Therapy System in those countries.

‡ As of 8/22/96, only 70 patients had been implanted long enough to reach the two-year treatment period; 58 of the 70 were continuing.

§ As of 8/22/96, only 24 patients had been implanted long enough to reach the three-year treatment period; 21 of the 24 were continuing.

Table 7 shows the number of patients included in the efficacy analysis. It is apparent from the table that not all continuing patients were used in the efficacy analysis. This difference was mostly because of missing data (some patients kept only sporadic records over the long term), although two patients were not used because they had had lobectomy surgery, which had affected their seizure rates.

Table 7. Patients Used for Efficacy Analysis

Study	E01	E02	E03	E04	Total
No. of patients randomized/stimulated	10	5	115	123	253
No. of patients entering long-term phase	10	5	113	123	251
No. of patients used in 1-year efficacy analysis/ No. Stimulated	10/10	4/5	102/111	86/112	202/238
No. of patients used in 2-year efficacy analysis/ No. Stimulated	8/9	2/4	51/71*	34/58†	95/142
No. of patients used in 3-year efficacy analysis/ No. Stimulated	4/7	2/3	49/57	0‡	55/67

* Of the 71 patients continuing, efficacy data were available for only 51.

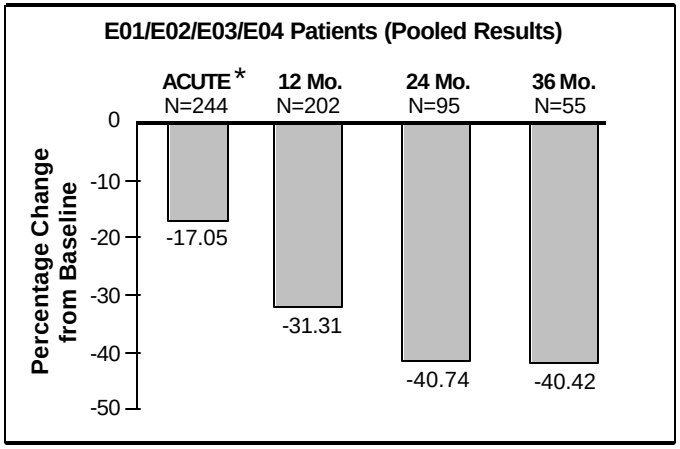
† Of the 58 patients, efficacy data were available for only 34.

‡ No data were available at the three-year time for the E04 patients.

7.1.1. Long-Term Results

Available long-term data from uncontrolled, open-label protocols during which antiepileptic drug and VNS Therapy device setting changes were allowed suggest improved efficacy over the first 24 months of treatment, with stabilization of this improvement after two years (see Figure 3). As evident from Table 7, these long-term data are limited at years two and three, with no patients being represented in the three-year analysis from Studies E04 or E05. There can be no assurances that the efficacy of the VNS Therapy treatment will continue to improve or will not decline over time, nor can there be assurances that additional long-term data will not reveal new adverse information presently unknown to Cyberonics. However, currently available long-term data do not suggest an increase or a worsening of adverse events, or a decline in efficacy.

Figure 3. Median Percentage Change in Seizure Frequency



* The acute phase results include seizure frequencies of the E03 Study LOW stimulation group, which included one-half the E03 patients, N=57. Patients were permitted to change their AEDs during these long-term follow-up studies, and these changes may have contributed to the change in seizure frequency.

7.2. Other Information

In the United States, the VNS Therapy System is approved for use in adults and adolescents over 12 years of age with partial onset seizures that are refractory to antiepileptic medications. Unlike the two randomized studies, Study E04, an open-label safety study, included patients 12 years old and younger, and patients with generalized seizures. Sixteen patients under age 12, ranging from 3.6 to 12 years old, were evaluated. (Two additional patients had unevaluable seizure data.) These patients were found to have a 17.9 percent median decrease in seizures during the acute phase, with 31 percent of the patients experiencing a greater than 50 percent decrease.

Additionally, 25 patients with generalized seizures were evaluated. (Two additional patients had unevaluable seizure data.) These patients were found to have a 46.6 percent median decrease in seizures during the acute phase, with 44 percent experiencing a greater than 50 percent decrease. The E04 results (N=116 analyzed), including patients younger than 12 and those with generalized seizures, showed a 22 percent median decrease during the acute phase, with 29 percent of the patients experiencing a greater than 50 percent decrease.

The E04 results (N=86 analyzed), excluding patients younger than 12 and those with generalized seizures, showed an 18.3 percent median decrease in seizures during the acute phase, with 27.9 percent of the patients experiencing a greater than 50 percent decrease.

7.3. Bibliography

A bibliography of animal and clinical studies is available from Cyberonics on request.

8. INDIVIDUALIZATION OF TREATMENT

Patients should be started on stimulation at a low current setting (0.25 mA), and the current should be increased gradually to allow accommodation to the stimulation. For patient comfort, the output current should be increased in 0.25 mA increments until a comfortable tolerance level is reached. Physicians should appreciate that some patients will accommodate to stimulation levels over time and should therefore allow further increases (in 0.25 mA steps) in output current, if needed. (See the Model 250 Software Physician's Manual.)

Table 8 lists the stimulation parameters used in the randomized, blinded, active control trials.

Table 8. High Stimulation Parameters (Optimal)

Stimulation Parameters	Normal Mode	Magnet Mode
Output current	0–3.5 mA	0–3.5 mA
Frequency	30 Hz	30 Hz
Pulse width	500 ? sec	500 ? sec
ON time	30 sec	30 sec
OFF time	5 min	N/A

The magnet output current should be set to a level that can be perceived by the patient to allow for daily testing of Pulse Generator operation.

⚠ The safety and efficacy of this therapy have not been systematically established for uses not covered in the "Intended Use / Indications" section of this manual or in patients with the following conditions:

- Cardiac arrhythmias or other abnormalities
- History of dysautonomias
- History of previous therapeutic brain surgery
- History of respiratory diseases or disorders, including dyspnea and asthma
- History of ulcers (gastric, duodenal, or other)
- History of vasovagal syncope
- Neurological diseases other than epilepsy
- Only one vagus nerve
- Other concurrent forms of brain stimulation
- Pre-existing hoarseness
- Pregnancy or nursing*

*Pre-clinical Study, Teratogenic Effects: There are no adequate and well-controlled studies of VNS Therapy in pregnant women. Reproduction studies have been performed using female rabbits stimulated with the commercially available VNS Therapy System at stimulation dose settings similar to those used for humans. These animal studies have revealed no evidence of impaired fertility or harm to the fetus due to VNS Therapy. Because animal reproduction studies are not always predictive of human response and animal studies cannot address developmental abnormalities, VNS should be used during pregnancy only if clearly needed. Although the operating ranges of the VNS Therapy System and fetal monitors are dissimilar and no interaction would be expected, testing has not been performed. Therefore, the potential may exist for interaction between the VNS Therapy System and fetal monitoring systems.

Additionally, further studies are planned for systematically establishing the therapy's use in the United States in patients younger than 12 or older than 60, and in those with primary generalized seizures.

9. PATIENT COUNSELING INFORMATION

Patients should be told to test their Pulse Generator's operation daily by performing magnet stimulation and verifying that stimulation occurs. If stimulation does not occur, their physician should be contacted.

It should be noted that the magnet stimulation timing is not synchronized with the timing clock used for determining ON time (see Figure 4) and has a tolerance of +/- 15% or +/-7 seconds. Therefore, if the magnet mode ON time is programmed to 7 seconds and the pulse generator is swiped at the end of the clock cycle, magnet stimulation may not be perceived by the patient. If the patient does not perceive the magnet stimulation, he or she should be instructed to swipe the pulse generator a second time.

In the unlikely event of uncomfortable adverse events, continuous stimulation, or other malfunction, the patient must be advised to hold or tape the magnet directly over the implanted Pulse Generator to prevent additional stimulation. If patients or caregivers find this procedure necessary, they should immediately notify the patient's physician.

10. CONFORMANCE TO STANDARDS

The VNS Therapy System conforms to the following standards:

- American National Standards Institute (ANSI) and Association for the Advancement of Medical Instrumentation (AAMI) NS15 — Implantable, peripheral nerve stimulators
- EN 45502-1 — Active Implantable Medical Devices: Requirements for the safety, marking, and information to be provided by the manufacturer

11. HOW SUPPLIED

Implantable portions of the VNS Therapy System have been sterilized using ethylene oxide gas (EO), and are supplied in a sterile package for direct introduction into the operating field. A process indicator is included in the package; devices should be implanted only if the indicator is green. An expiration date is marked on the outer package.

If the package has been exposed to extreme temperatures or moisture (see the section on “Sterilization, Storage, and Handling” in this manual) or if there is any indication of external damage, the package should be left unopened and returned to Cyberonics.

12. OPERATOR'S MANUAL

12.1. Directions for Use

12.1.1. Specifications and Product Information

The specifications and product information for the VNS Therapy Pulse Generators are presented in Table 9:

Table 9. Specifications and Product Information

Stimulation Parameters	Available Parameter Settings
Output current	0-3.5 mA in 0.25-mA steps* ? 0.25 ? 1 mA, ? 10% > 1 mA
Signal frequency	1, 2, 5, 10, 15, 20, 25, 30 Hz, ?6%
Pulse width	130, 250, 500, 750, 1000 ? sec ? 10%
Signal ON time	7, 14, 21, 30, 60 sec ?15% or + 7 sec, whichever is greater (?15% or ? 7 sec in Magnet Mode)
Signal OFF time	0.2, 0.3, 0.5, 0.8, 1.1, 1.8, 3 min, and 5 to 180 min (5 to 60 in 5-min steps; 60 to 180 in 30-min steps), +4.4 / -8.4 sec
Magnet activation	Provided by magnet application (output current, pulse width, and signal ON time may be independently programmed for this purpose)
Reset parameters	0 mA; 10 Hz; 500 ? sec; ON time, 30 sec; OFF time, 60 min
Nominal Parameters	0 mA; 30 Hz; 500 ? sec; ON time, 30 sec; OFF time, 10 min
Telemetry Reports	
Device History Report	Patient code, implant date, model number, and serial number
Device Diagnostic Report	Status messages for programming, telemetry, ERI, output current, Lead impedance, DC-DC converter value, programmed amplitude, and device treatment status
Power Source	
(All Serial Numbers)	
Battery	Wilson Greatbatch Ltd., Model 2075
Chemistry	Lithium carbon monofluoride
Voltage	3.3 V, open circuit
Rated capacity	1.7 ampere-hours
Self-discharge rate	? 1% per year

Physical Characteristics		
Materials		
Case	Titanium, hermetically sealed	
Header	Polyurethane--Tecothane? TT-1075D-M Thermoplastic	
Lead connector blocks	Stainless steel	
Setscrew plug(s)	Silicone†	
Measurements (Typical)		
	Model 102	***Model 102R***
Lead receptacle(s)	0.126 in. (3.2 mm) nominal	0.2 in. (5 mm) nominal
Dimensions	2.0 in. x 2.0 in. x.27 in. (52 mm x 52 mm x 6.9 mm)	2.0 in. x 2.3 in. x .27 in. (52 mm x 58.4 mm x 6.9 mm)
Weight	0.88 oz. (25 g)	0.95 oz. (27 g)
Connector Retention Strength		
With VNS Therapy Lead	> 10N	
Serial Number Range		
Model 102	< 1000000	
Model 102R	? 1000000	

* For output currents ? 1mA, the tolerance is ±.25mA. Maximum output is 12.5±2.5 volts with the exception of 10 Hz, 7 sec On Time the maximum output is 4.4 volts and .25mA tolerance. This .25mA tolerance also applies to 15 Hz, 7 sec On Time, .5mA output current.

† Latex is not included in any component of the VNS Therapy System.

12.1.2 Operating Characteristics

12.1.2.1. Communicating with the VNS Therapy System

A Model 200 or 201 Programming Wand connected to a compatible computer running the Model 250 Software is needed to communicate with the Pulse Generator. (See the Model 250 Software Physician's Manual, Version 6.1 or Version 4.6 for a list of compatible computers.)

(For proper placement of the Programming Wand, connection of the Wand to the computer, and use of the Wand, see the Model 200 or 201 Programming Wand Physician's Manual. For proper use of the Software, see the Model 250 Software Physician's Manual.)

After the program has been initiated, software screens display prompts and messages to aid in communicating with the Pulse Generator.

The Pulse Generator "listens" for a communication signal for a 300-msec period every 6.8 seconds. Communication usually takes between three and 10 seconds but may be prolonged in the presence of electromagnetic interference (EMI). The Pulse Generator listens for and implements interrogations, parameter programming instructions, requests for Device Diagnostics testing, and Device History inquiries. In response, the Pulse Generator transmits information on the stimulation parameter settings, changes its parameter settings, responds to requests for Device Diagnostics testing, and provides Device Histories, respectively.

Each time these data are transmitted by the Pulse Generator, they are saved by the Software to databases on the storage disk. (See the Model 250 Software Physician's Manual for details on viewing the database information.)

The Pulse Generator also transmits a signal for use in evoked potential monitoring.

In addition to the Software and Programming Wand combination, a magnet can be used for one-way communication to the Pulse Generator by activating a reed switch in the electronic circuitry. The magnet can be used to initiate stimulation, temporarily inhibit stimulation, perform Magnet Mode diagnostics, and reset the Pulse Generator.

12.1.2.2.Stimulation

After the Pulse Generator has been programmed, the stimulation will repeat in accordance with the programmed ON and OFF cycle until the Pulse Generator receives communication from the VNS Therapy programming system or until it is activated or inhibited with a magnet. Immediately after successful programming, the Pulse Generator delivers a programmed stimulation that enables patient response to be evaluated. If programming is performed during stimulation, stimulation will be terminated; after programming, stimulation will begin, using the revised settings.

The Pulse Generator operation described in the preceding paragraph is done in Normal Mode. A Magnet Mode stimulation is a single stimulation initiated by applying or passing a magnet over the Pulse Generator for at least one second and then immediately removing it from the area over the Pulse Generator. Stimulation is delivered after the magnet is removed. The Magnet Mode uses the same frequency as the Normal Mode, but the output current, pulse width, and signal ON time are independently programmable.

An interrogation is made to determine the present settings of the stimulation parameters. If interrogation is made during stimulation, completion of stimulation will be delayed until the interrogation is finished.

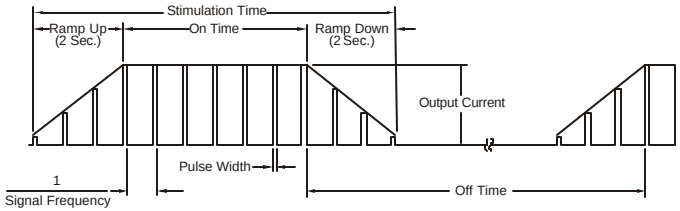
A graphic representation of stimulation (Figure 4) depicts the relationship of the stimulation programmable parameters. The programmable parameters are independently variable, offering multiple setting combinations from which the physician may select optimal stimulation for the patient. Figure 4 shows that the output pulse can be varied both by amplitude (output current) and duration (pulse width). The number of output pulses delivered per second determines the frequency.

The percentage of time the Pulse Generator is stimulating is called a “duty cycle.” A duty cycle is calculated by dividing the stimulation time (programmed ON time plus two seconds of ramp-up time and two seconds of ramp-down time) by the sum of the ON and OFF times. The various parameter settings for stimulation are listed in the “Specifications and Product Information” section of this manual.

When selecting a combination of parameter settings that will deliver optimal stimulation, the physician should also consider that some combinations will decrease battery life faster than others. (See the “Effects of Programmed Settings on Pulse Generator Projected Lifetime” section of this manual.)

⚠ Stimulation with an ON time ? OFF time has resulted in degenerative nerve damage in laboratory animals. ON time ? OFF time can be simulated by very frequent magnet activation. Cyberonics recommends that stimulation at these combinations of ranges be avoided.

Figure 4. Stimulation (All Duty Cycles Except Low-Output ? 10 Hz)



12.1.2.2.1. Initiating Stimulation with a Magnet

There are four possible uses of the magnet:

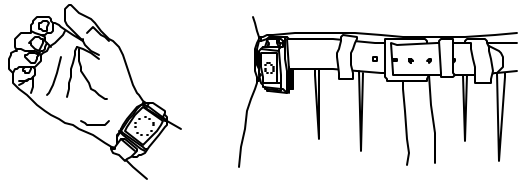
? ? To provide on-demand stimulation as an attempt to abort or de-intensify an oncoming seizure

? ? To temporarily inhibit stimulation

? ? To reset the Pulse Generator (in combination with the Programming Wand)

? ? To test daily the functioning of the Pulse Generator Cyberonics recommends that patients be instructed to use the magnet to activate stimulation during an aura or at the start of a seizure. Magnet activation may be initiated by the patient, a companion, or the physician by applying or passing a magnet over the Pulse Generator to activate a reed switch in the Pulse Generator's electronic circuitry. This action changes the Pulse Generator from Normal Mode to Magnet Mode. Two identical magnets (shown in Figure 5), each providing a minimum of 50 gauss at 1 inch, are supplied by Cyberonics. A Cyberonics watch-style magnet attaches to a wristband in the same manner as a wristwatch, and a Cyberonics pager-style magnet attaches to a belt in the same manner as a pager with a quick-release mechanism.

Figure 5. Magnet Styles



Cyberonics Magnet
(watch-style)

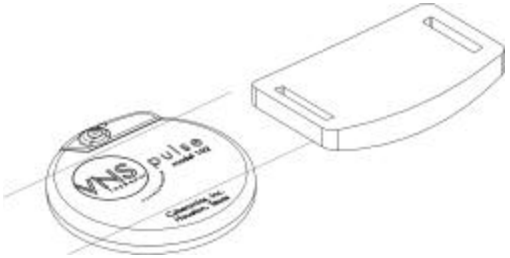
Cyberonics Magnet
(pager-style)

The proper orientation and motion for initiating magnet activation is shown in Figure 6. The magnet is shown without the belt clip or wristband to illustrate the proper orientation of the magnet to the Pulse Generator.

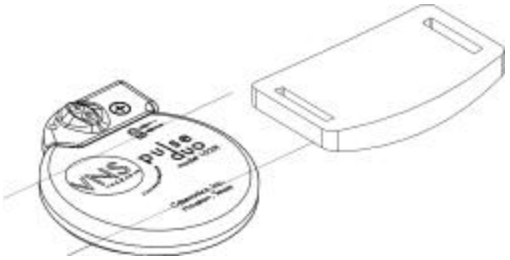
⚠ Physicians should warn patients against excessive or continuous use (?8 hours) of magnet-activated stimulation since this could result in exceeding the 50 percent duty cycle and could damage the patient's left vagus nerve.

Figure 6. Initiating Magnet Activation

Model 102



Model 102R



⚠ Label side of magnet should face the Puls e Generator while activating or stopping stimulation.

All magnets may lose their effectiveness over time. Avoid dropping the magnets or storing them near other magnets.

To initiate stimulation, apply or pass the magnet over the Pulse Generator for at least one second, and then immediately remove it from the area over the Pulse Generator. Removal of the magnet causes the Pulse Generator to operate in Magnet Mode, delivering a single stimulation having the programmed magnet pulse width, magnet current, and magnet signal ON time settings. The frequency is the programmed value for Normal Mode. Any Normal Mode programmed stimulation will always be overridden by a Magnet Mode, even if the Magnet Mode output current is set to 0 mA. If Magnet Mode stimulation is not desired, the Magnet Mode output current may be programmed to 0 mA. Magnet use does not restart the normal OFF time. Therefore, depending on the timing of the magnet use, the patient could receive a second stimulation quickly after magnet activation.

Cyberonics recommends that testing of the magnet output be performed while the patient is still in the physician's office to ensure tolerability of the magnet output.

12.1.2.2.2 Inhibiting Pulse Generator Output with a Magnet

Application of the magnet during stimulation will inhibit the output. In addition, holding the magnet in place for at least 65 seconds will prevent the initiation of a Magnet Mode stimulation and will terminate any ongoing Normal Mode stimulation. After the magnet is removed, Normal Mode operation will resume with stimulation when one complete OFF time has elapsed. In the unlikely event of continuous stimulation or other malfunction, the patient must be advised to apply the magnet, secure it in place, and immediately notify his or her physician.

⚠ **If stimulation becomes painful,** the patient should be instructed to stop the stimulation with the magnet.

12.1.2.2.3. Resetting the Microprocessor Using a Magnet and the Programming Wand

The VNS Therapy System allows the Pulse Generator microprocessor to be reset in the event of a malfunction. Resetting will be necessary only in the rare case of microprocessor memory malfunction, which might be caused by conditions described in the “Environmental Hazards” section of this manual. Microprocessor reset is indicated when communication with the Pulse Generator becomes impossible. (See the “Troubleshooting” section of the Model 200 or 201 Programming Wand Physician’s Manual and the “Precautions and Troubleshooting” section of the Model 250 Software Physician’s Manual for suggestions in solving communication difficulties.)

For instructions on resetting the microprocessor, refer to the Model 200 or 201 Programming Wand Physician's Manual. It is recommended, except in cases of a medical emergency, that the physician consults a Cyberonics technical representative before resetting is performed.

⚠ When the Pulse Generator is reset, all device history information is lost, and the reset parameters (0 mA, 10 Hz; 500 ?sec; ON time, 30 sec; OFF time, 60 min) are internally programmed. Resetting the Pulse Generator turns the device off (output current = 0 mA). After a successful reset, the Pulse Generator patient code must be re-entered, and the Pulse Generator reprogrammed to the desired parameters.

12.1.2.3.Device History

The Device History consists of the Pulse Generator serial number, model number, the patient code (usually three initials), implantation date, and other information pertinent to diagnostic and programming events. Use the Software to access and view Device History information.

12.1.2.4.Device Diagnostics

Information from Pulse Generator diagnostic tests aids the physician in determining if the Pulse Generator is operating properly before it is implanted, if the Pulse Generator output current is being delivered at the programmed value, if Lead impedance is within an acceptable range, and in which mode the Pulse Generator is operating. (Details of the available diagnostic tests are found in the Model 250 Software Physician's Manual.)

12.1.2.4.1. Reasons for High Lead Impedance Readings

The Lead Test is the most appropriate of the device diagnostic tests to evaluate Lead impedance for the VNS Therapy System. The Lead Test is performed at 1.0 mA, 500 ?sec. Use Table 10 to find the DC-DC Converter Code displayed by the Lead Test diagnostic screen to determine an estimate of Lead impedance in k ohms.

Using Table 10 with the DC-DC Converter Code from diagnostic screens other than the Lead and Pre-implant tests is not appropriate unless the Pulse Generator output parameters are the values indicated in the tables. High Lead impedance is defined as any DC-DC Converter Code greater than or equal to four with 1 mA of diagnostic current.

Table 10. DC-DC Converter Codes and Lead Impedance (Models 102 and 102R)

DC-DC Converter Code[1]	Estimated Lead Impedance[2]
	1mA, 500 ? sec
0	? 1.7 k ohms
1	1.7-2.7 k ohms
2	2.7-4.0 k ohms
3	4.0-5.5 k ohms
4	5.5-7 k ohms
5	7-8 k ohms
6	8-9 k ohms
7	? 9 k ohms

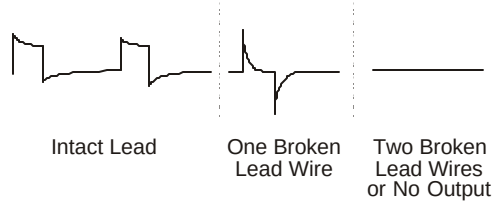
1 DC-DC Converter Codes are displayed during Lead Test diagnostics.
2 Tolerance is ? 10 percent.

⚠ **Possible causes of high Lead impedance readings** are thought to include fibrosis between the nerve and the electrode, Lead fracture, Lead disconnection from the Pulse Generator, and high battery impedance approaching end of service (EOS).

High Lead impedance, in the absence of other device-related complications, is not an indication of a Lead or Pulse Generator malfunction. High Lead impedance in combination with the patient's failure to feel even the maximum output stimulus may indicate a Lead wire fracture or other type of electrical discontinuity in the Lead. (See the Model 250 Software Physician's Manual for additional instructions on performing the Lead Test.) Patients experiencing high Lead impedance, no sensation of maximum output stimulation, and an increase in seizures should be further evaluated for possible Lead replacement.

Either evoked potential monitoring equipment or an oscilloscope can be used to analyze the stimulus waveform from the neck for verification of an electrical discontinuity. A differentiated waveform with narrowed pulses or no wave form at all can confirm a discontinuity. Figure 7 shows simulated waveforms expected from skin electrodes for a Lead that is intact and for a Lead that has a fracture in one or both wires. In addition to these approaches, Lead fractures can sometimes be identified in x-rays of the implant site.

Figure 7. Typical Waveforms Obtained from Skin Electrodes



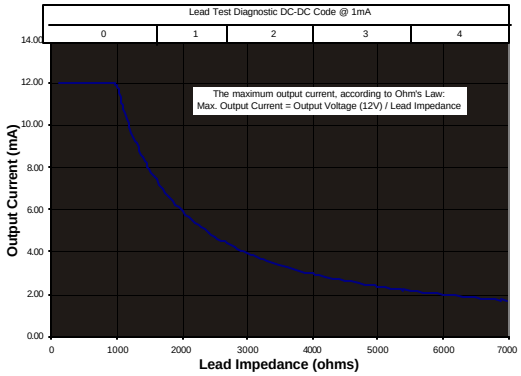
12.1.2.5 Delivery of Programmed Output Current

If the diagnostic tests indicate the output current is LIMIT, the Pulse Generator may not deliver the programmed output current. Reasons for failure to deliver the programmed output current include a high output current, high Lead impedance, and low battery voltage. Figure 8 demonstrates the relationship of Lead impedance to maximum deliverable output current.

If the Pulse Generator is failing to deliver the programmed output current, the physician can reprogram to a lower output current and attempt to compensate for a decrease in delivered energy by widening the pulse width. For example, if the output current is at LIMIT for a Pulse Generator programmed at 2.5 mA, 30 Hz, 500 ?sec with 30 seconds ON time, then the parameters may be changed by lowering the output current to 2.0 mA and widening the pulse width to 750 ?sec.

Figure 8. Relationship of Lead Impedance to Maximum Deliverable Output Current

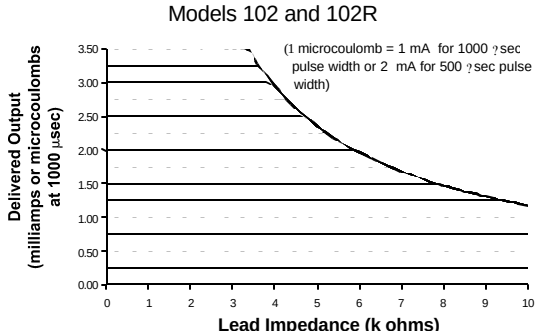
Models 102 and 102R



12.1.2.6 Charge Delivered Per Pulse

The charge delivered per pulse is the parameter most important in evaluating stimulation output. It is defined as a microcoulomb (?C), which is the product of current and time—that is, the output current (mA) multiplied by the pulse width (msec). Figure 9 shows the relationship of programmed output current (?C) to Lead impedance for an output current of 0 to 3.5 mA.

Figure 9. Relationship of Programmed Output Current to Lead Impedance



⚠ **Do not use frequencies of 5 Hz or below for long-term stimulation.** Because these frequencies generate an electromagnetic trigger signal, their use results in excessive battery depletion of the implanted Pulse Generator and, therefore, should be used for short periods of time only.

12.1.2.7. Effects of Programmed Settings on Pulse Generator Projected Lifetime

The choice of settings for output parameters affects Pulse Generator battery life. Generally, a high duty cycle will deplete the battery over a shorter period of time than a low duty cycle will. Table 11 shows duty cycles for typical ON time and OFF time settings (except for frequency settings ? 10 Hz). A typical two-second ramp-up time and two-second ramp-down time are present for most stimulations except those set at some low output currents and below 10 Hz. As depicted in the graphic representation of stimulation in Figure 4, neither of these two-second intervals is considered part of the programmed ON time; however, they are included in calculations for determining the percentage of stimulation time (duty cycle) and predicting battery life.

Table 11. Duty Cycles for Various ON and OFF

Duty Cycles* (% ON Time)									
ON Time (sec)	OFF Time (min)								
	0.2	0.3	0.5	0.8	1.1	1.8	3	5	10
7	58%	44%	30%	20%	15%	10%	6%	4%	2%
14	69	56	41	29	23	15	9	6	3
21	76	64	49	36	29	19	12	8	4
30	81	71	57	44	35	25	16	10	5
60	89	82	71	59	51	38	27	18	10

* A duty cycle is calculated by dividing stimulation time (programmed ON time plus two seconds of ramp-up time and two seconds of ramp-down time) by the sum of the ON time and OFF time.

For the Models 102 and 102R, the approximate battery lifetime predicted at programmed settings of 20 Hz with a 500 ?sec pulse width and 2 mA output current, a Lead impedance of 4 k ohms, and a duty cycle of 10 percent is 8.4 years (100.8 months).

Tables 12 and 13 provide estimated battery lifetimes under a variety of stimulation conditions, including Lead impedance. Because of the number of possible parameter combinations, it is impractical to provide the projected life for all possible combinations. The tables should not be used to predict battery end of service, but they give some indication of the effect of various parameter changes on battery life and can be used to assist in the selection of parameter settings. They also indicate that battery life can be maximized at low duty cycles and low frequencies (10 to 20 Hz) for stimulation.

Table 12. Estimated Battery Life - Nominal Longevity Estimates Beginning of Life (BOL) to End of Service (EOS)

Frequency	Pulse Width	Output Current	Load	Nominal Estimated Battery Life (Yrs)		
				10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
Hz.	uSec.	mA	k ohms	Life (yrs)	Life (yrs)	Life (yrs)
10	130	1	3	16.8	13.1	11.2
10	130	1	4	16.7	12.7	10.8
10	130	1	5	16.0	11.5	9.5
10	130	1	7	15.2	10.3	8.3
10	130	1	9	14.3	9.0	7.1
10	130	1.5	3	15.6	10.8	8.8
10	130	1.5	4	15.2	10.3	8.3
10	130	1.5	5	14.8	9.7	7.7
10	130	1.5	7	13.8	8.4	6.5
10	130	1.5	9	13.8	8.4	6.5
10	130	2	3	15.1	10.1	8.1
10	130	2	4	14.5	9.3	7.3
10	130	2	5	13.5	8.0	6.1
10	130	2	7	13.7	8.2	6.3
10	130	2	9	13.9	8.5	6.6
10	130	3.5	3	12.7	7.1	5.3
10	130	3.5	4	12.8	7.2	5.5
10	130	3.5	5	13.0	7.5	5.7

Frequency	Pulse Width	Output Current	Load	Nominal Estimated Battery Life (Yrs)		
				10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
Hz.	uSec.	mA	k ohms	Life (yrs)	Life (yrs)	Life (yrs)
10	130	3.5	7	13.6	8.1	6.2
10	130	3.5	9	13.9	8.5	6.6
10	500	1	3	15.2	10.3	8.3
10	500	1	4	15.0	10.0	8.0
10	500	1	5	14.4	9.1	7.2
10	500	1	7	13.3	7.7	5.9
10	500	1	9	12.5	6.9	5.2
10	500	1.5	3	13.7	8.2	6.3
10	500	1.5	4	12.9	7.3	5.5
10	500	1.5	5	12.1	6.5	4.8
10	500	1.5	7	10.7	5.3	3.9
10	500	1.5	9	11.3	5.8	4.2
10	500	2	3	12.2	6.6	5.0
10	500	2	4	11.3	5.8	4.3
10	500	2	5	10.0	4.7	3.4
10	500	2	7	10.3	5.0	3.6
10	500	2	9	11.1	5.6	4.1
10	500	3.5	3	8.0	3.4	2.4
10	500	3.5	4	8.4	3.7	2.6
10	500	3.5	5	9.0	4.1	2.9
10	500	3.5	7	9.8	4.6	3.3

Frequency	Pulse Width	Output Current	Load	Nominal Estimated Battery Life (Yrs)		
				10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
Hz.	uSec.	mA	k ohms	Life (yrs)	Life (yrs)	Life (yrs)
10	500	3.5	9	10.6	5.2	3.8
10	1000	1	3	13.3	7.7	5.9
10	1000	1	4	13.2	7.7	5.9
10	1000	1	5	12.4	6.8	5.1
10	1000	1	7	10.9	5.4	4.0
10	1000	1	9	10.1	4.8	3.5
10	1000	1.5	3	11.4	5.9	4.3
10	1000	1.5	4	10.6	5.2	3.8
10	1000	1.5	5	9.7	4.5	3.2
10	1000	1.5	7	8.4	3.6	2.6
10	1000	1.5	9	8.7	3.9	2.8
10	1000	2	3	9.7	4.5	3.3
10	1000	2	4	8.3	3.6	2.5
10	1000	2	5	7.3	3.0	2.1
10	1000	2	7	7.8	3.3	2.3
10	1000	2	9	8.5	3.7	2.6
10	1000	3.5	3	5.2	1.9	1.3
10	1000	3.5	4	5.8	2.2	1.5
10	1000	3.5	5	6.4	2.5	1.7
10	1000	3.5	7	7.4	3.1	2.1
10	1000	3.5	9	8.1	3.4	2.4

Frequency	Pulse Width	Output Current	Load	Nominal Estimated Battery Life (Yrs)		
				10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
Hz.	uSec.	mA	k ohms	Life (yrs)	Life (yrs)	Life (yrs)
20	130	1	3	15.8	11.2	9.2
20	130	1	4	15.2	10.2	8.2
20	130	1	5	14.6	9.4	7.4
20	130	1	7	13.6	8.1	6.2
20	130	1	9	12.7	7.1	5.4
20	130	1.5	3	14.0	8.6	6.7
20	130	1.5	4	13.4	7.9	6.0
20	130	1.5	5	12.7	7.1	5.4
20	130	1.5	7	11.6	6.0	4.4
20	130	1.5	9	11.7	6.2	4.6
20	130	2	3	13.1	7.6	5.8
20	130	2	4	12.3	6.7	5.0
20	130	2	5	11.2	5.7	4.2
20	130	2	7	11.5	6.0	4.4
20	130	2	9	11.9	6.3	4.7
20	130	3.5	3	9.9	4.7	3.4
20	130	3.5	4	10.2	4.9	3.5
20	130	3.5	5	10.6	5.2	3.8
20	130	3.5	7	11.1	5.6	4.1
20	130	3.5	9	11.6	6.1	4.5
20	500	1	3	13.0	7.5	5.7

Frequency	Pulse Width	Output Current	Load	Nominal Estimated Battery Life (Yrs)		
				10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
Hz.	uSec.	mA	k ohms	Life (yrs)	Life (yrs)	Life (yrs)
20	500	1	4	12.8	7.2	5.5
20	500	1	5	11.4	5.9	4.4
20	500	1	7	10.6	5.2	3.8
20	500	1	9	9.8	4.6	3.3
20	500	1.5	3	11.1	5.6	4.1
20	500	1.5	4	10.1	4.9	3.5
20	500	1.5	5	9.3	4.3	3.1
20	500	1.5	7	8.0	3.4	2.4
20	500	1.5	9	8.5	3.7	2.6
20	500	2	3	9.4	4.3	3.1
20	500	2	4	8.4	3.7	2.6
20	500	2	5	7.2	2.9	2.0
20	500	2	7	7.7	3.2	2.3
20	500	2	9	8.3	3.6	2.5
20	500	3.5	3	5.4	2.0	1.4
20	500	3.5	4	5.8	2.2	1.5
20	500	3.5	5	6.4	2.5	1.7
20	500	3.5	7	7.3	3.0	2.1
20	500	3.5	9	8.0	3.4	2.4
20	1000	1	3	10.0	4.8	3.4
20	1000	1	4	10.6	5.2	3.8

Frequency	Pulse Width	Output Current	Load	Nominal Estimated Battery Life (Yrs)		
				10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
Hz.	uSec.	mA	k ohms	Life (yrs)	Life (yrs)	Life (yrs)
20	1000	1	5	9.7	4.5	3.3
20	1000	1	7	8.2	3.5	2.5
20	1000	1	9	7.1	2.9	2.0
20	1000	1.5	3	8.5	3.7	2.6
20	1000	1.5	4	7.6	3.2	2.2
20	1000	1.5	5	6.8	2.8	1.9
20	1000	1.5	7	5.6	2.1	1.5
20	1000	1.5	9	6.1	2.4	1.6
20	1000	2	3	6.6	2.6	1.8
20	1000	2	4	5.3	2.0	1.4
20	1000	2	5	4.8	1.7	1.2
20	1000	2	7	5.3	2.0	1.3
20	1000	2	9	5.9	2.3	1.6
20	1000	3.5	3	3.1	1.1	0.7
20	1000	3.5	4	3.6	1.2	0.8
20	1000	3.5	5	4.1	1.4	1.0
20	1000	3.5	7	4.9	1.8	1.2
20	1000	3.5	9	5.6	2.1	1.4
30	130	1	3	14.9	9.9	7.9
30	130	1	4	14.5	9.2	7.2
30	130	1	5	13.4	7.9	6.0

Frequency	Pulse Width	Output Current	Load	Nominal Estimated Battery Life (Yrs)		
				10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
Hz.	uSec.	mA	k ohms	Life (yrs)	Life (yrs)	Life (yrs)
30	130	1	7	12.3	6.7	5.0
30	130	1	9	11.5	6.0	4.4
30	130	1.5	3	12.8	7.2	5.5
30	130	1.5	4	12.2	6.6	4.9
30	130	1.5	5	11.6	6.0	4.4
30	130	1.5	7	10.3	5.0	3.6
30	130	1.5	9	10.5	5.2	3.7
30	130	2	3	11.7	6.2	4.6
30	130	2	4	10.9	5.5	4.0
30	130	2	5	9.6	4.5	3.2
30	130	2	7	9.9	4.7	3.4
30	130	2	9	10.3	5.0	3.6
30	130	3.5	3	8.2	3.5	2.5
30	130	3.5	4	8.5	3.7	2.6
30	130	3.5	5	9.0	4.0	2.9
30	130	3.5	7	9.6	4.4	3.2
30	130	3.5	9	10.0	4.7	3.4
30	500	1	3	11.1	5.7	4.1
30	500	1	4	10.9	5.4	4.0
30	500	1	5	10.3	5.0	3.6
30	500	1	7	8.8	3.9	2.8

Frequency	Pulse Width	Output Current	Load	Nominal Estimated Battery Life (Yrs)		
				10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
Hz.	uSec.	mA	k ohms	Life (yrs)	Life (yrs)	Life (yrs)
30	500	1	9	8.0	3.4	2.4
30	500	1.5	3	9.3	4.2	3.0
30	500	1.5	4	8.5	3.7	2.6
30	500	1.5	5	7.7	3.2	2.3
30	500	1.5	7	6.4	2.5	1.8
30	500	1.5	9	6.9	2.8	1.9
30	500	2	3	7.5	3.1	2.2
30	500	2	4	6.5	2.6	1.8
30	500	2	5	5.6	2.1	1.5
30	500	2	7	6.1	2.4	1.6
30	500	2	9	6.7	2.7	1.9
30	500	3.5	3	4.0	1.4	1.0
30	500	3.5	4	4.4	1.6	1.1
30	500	3.5	5	4.9	1.8	1.2
30	500	3.5	7	6.3	2.5	1.7
30	500	3.5	9	6.4	2.5	1.8
30	1000	1	3	8.9	4.0	2.8
30	1000	1	4	8.3	3.6	2.5
30	1000	1	5	8.0	3.4	2.4
30	1000	1	7	6.5	2.6	1.8
30	1000	1	9	5.5	2.1	1.4

Frequency	Pulse Width	Output Current	Load	Nominal Estimated Battery Life (Yrs)		
				10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
Hz.	uSec.	mA	k ohms	Life (yrs)	Life (yrs)	Life (yrs)
30	1000	1.5	3	6.3	2.5	1.7
30	1000	1.5	4	5.9	2.3	1.6
30	1000	1.5	5	5.2	2.0	1.3
30	1000	1.5	7	4.2	1.5	1.0
30	1000	1.5	9	4.7	1.7	1.2
30	1000	2	3	5.0	1.8	1.3
30	1000	2	4	3.9	1.4	0.9
30	1000	2	5	3.5	1.2	0.8
30	1000	2	7	4.0	1.4	0.9
30	1000	2	9	4.5	1.6	1.1
30	1000	3.5	3	2.2	0.7	0.5
30	1000	3.5	4	2.7	0.9	0.6
30	1000	3.5	5	3.0	1.0	0.7
30	1000	3.5	7	3.6	1.3	0.9
30	1000	3.5	9	4.2	1.5	1.0

Table 13. Estimated Battery Life - Worst Case Longevity Estimates BOL to ERI

				Worst Case Estimated Battery Life(Yrs)		
Frequency (Hz)	Pulse Width (? sec)	Output Current (mA)	Load Resistance (K?)	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
10	130	1	3	10.4	7.3	5.9
10	130	1	4	10.7	7.7	6.4
10	130	1	5	10.0	6.6	5.3
10	130	1	7	9.4	5.8	4.5
10	130	1	9	8.3	4.6	3.4
10	130	1.5	3	8.9	5.2	4.0
10	130	1.5	4	9.4	5.8	4.5
10	130	1.5	5	9.3	5.7	4.4
10	130	1.5	7	8.5	4.8	3.6
10	130	1.5	9	8.2	4.4	3.3
10	130	2	3	10.0	6.6	5.3
10	130	2	4	9.6	6.1	4.8
10	130	2	5	8.4	4.7	3.5
10	130	2	7	8.9	5.2	4.0
10	130	2	9	9.4	5.8	4.5
10	130	3.5	3	7.9	4.2	3.1
10	130	3.5	4	8.1	4.4	3.3
10	130	3.5	5	8.3	4.5	3.4
10	130	3.5	7	8.8	5.1	3.9

				Worst Case Estimated Battery Life(Yrs)		
Frequency (Hz)	**Pulse Width (? sec)**	**Output Current (mA)**	**Load Resistance (K?)**	**10% Duty Cycle**	**33% Duty Cycle**	**50% Duty Cycle**
10	130	3.5	9	9.4	5.8	4.5
10	500	1	3	9.4	5.8	4.5
10	500	1	4	9.9	6.4	5.1
10	500	1	5	9.3	5.6	4.4
10	500	1	7	8.5	4.8	3.6
10	500	1	9	7.8	4.1	3.1
10	500	1.5	3	8.4	4.6	3.5
10	500	1.5	4	8.1	4.4	3.3
10	500	1.5	5	8.0	4.3	3.2
10	500	1.5	7	7.3	3.7	2.7
10	500	1.5	9	7.2	3.6	2.6
10	500	2	3	8.0	4.3	3.2
10	500	2	4	6.8	3.3	2.3
10	500	2	5	6.5	3.1	2.2
10	500	2	7	6.8	3.2	2.3
10	500	2	9	6.3	2.9	2.1
10	500	3.5	3	5.6	2.4	1.7
10	500	3.5	4	5.4	2.3	1.6
10	500	3.5	5	6.2	2.8	2.0
10	500	3.5	7	6.2	2.8	2.0

				Worst Case Estimated Battery Life(Yrs)		
Frequency (Hz)	**Pulse Width (? sec)**	**Output Current (mA)**	**Load Resistance (K?)**	**10% Duty Cycle**	**33% Duty Cycle**	**50% Duty Cycle**
10	500	3.5	9	7.0	3.4	2.5
10	1000	1	3	8.0	4.2	3.1
10	1000	1	4	8.0	4.3	3.2
10	1000	1	5	7.7	4.0	2.9
10	1000	1	7	6.6	3.1	2.2
10	1000	1	9	5.9	2.6	1.9
10	1000	1.5	3	7.4	3.8	2.7
10	1000	1.5	4	7.2	3.6	2.6
10	1000	1.5	5	6.4	3.0	2.1
10	1000	1.5	7	5.8	2.5	1.8
10	1000	1.5	9	5.9	2.6	1.8
10	1000	2	3	6.5	3.1	2.2
10	1000	2	4	4.9	2.0	1.4
10	1000	2	5	4.7	1.9	1.3
10	1000	2	7	4.9	2.0	1.4
10	1000	2	9	5.5	2.4	1.7
10	1000	3.5	3	3.5	1.3	0.9
10	1000	3.5	4	3.9	1.5	1.0
10	1000	3.5	5	4.4	1.8	1.2
10	1000	3.5	7	5.0	2.1	1.4
10	1000	3.5	9	5.3	2.3	1.6

				Worst Case Estimated Battery Life(Yrs)		
Frequency (Hz)	**Pulse Width (? sec)**	**Output Current (mA)**	**Load Resistance (K?)**	**10% Duty Cycle**	**33% Duty Cycle**	**50% Duty Cycle**
20	130	1	3	9.9	6.4	5.1
20	130	1	4	9.2	5.6	4.3
20	130	1	5	9.7	6.2	4.9
20	130	1	7	8.8	5.1	3.9
20	130	1	9	8.7	5.0	3.8
20	130	1.5	3	9.0	5.4	4.1
20	130	1.5	4	8.7	5.0	3.8
20	130	1.5	5	8.1	4.3	3.2
20	130	1.5	7	7.3	3.7	2.7
20	130	1.5	9	7.7	4.0	3.0
20	130	2	3	8.6	4.9	3.7
20	130	2	4	7.0	3.4	2.5
20	130	2	5	7.0	3.4	2.5
20	130	2	7	7.4	3.7	2.7
20	130	2	9	7.8	4.1	3.1
20	130	3.5	3	6.5	3.1	2.2
20	130	3.5	4	6.9	3.3	2.4
20	130	3.5	5	7.2	3.6	2.6
20	130	3.5	7	7.3	3.6	2.6
20	130	3.5	9	7.9	4.2	3.1

				Worst Case Estimated Battery Life(Yrs)		
Frequency (Hz)	**Pulse Width (? sec)**	**Output Current (mA)**	**Load Resistance (K?)**	**10% Duty Cycle**	**33% Duty Cycle**	**50% Duty Cycle**
20	500	1	3	8.3	4.5	3.4
20	500	1	4	8.7	5.0	3.8
20	500	1	5	4.6	1.9	1.3
20	500	1	7	7.2	3.6	2.6
20	500	1	9	6.2	2.8	2.0
20	500	1.5	3	7.1	3.5	2.5
20	500	1.5	4	6.6	3.1	2.2
20	500	1.5	5	5.8	2.6	1.8
20	500	1.5	7	5.2	2.2	1.5
20	500	1.5	9	5.5	2.4	1.7
20	500	2	3	6.2	2.8	2.0
20	500	2	4	5.6	2.4	1.7
20	500	2	5	4.9	2.0	1.4
20	500	2	7	5.3	2.3	1.6
20	500	2	9	5.6	2.4	1.7
20	500	3.5	3	3.8	1.4	1.0
20	500	3.5	4	4.1	1.6	1.1
20	500	3.5	5	4.4	1.8	1.2
20	500	3.5	7	5.3	2.2	1.6
20	500	3.5	9	5.4	2.3	1.6
20	1000	1	3	3.9	1.5	1.0

				Worst Case Estimated Battery Life(Yrs)		
Frequency (Hz)	**Pulse Width (? sec)**	**Output Current (mA)**	**Load Resistance (K?)**	**10% Duty Cycle**	**33% Duty Cycle**	**50% Duty Cycle**
20	1000	1	4	6.6	3.1	2.2
20	1000	1	5	6.6	3.1	2.3
20	1000	1	7	5.9	2.6	1.8
20	1000	1	9	4.7	1.9	1.3
20	1000	1.5	3	5.7	2.5	1.8
20	1000	1.5	4	5.4	2.3	1.6
20	1000	1.5	5	4.7	1.9	1.3
20	1000	1.5	7	3.8	1.5	1.0
20	1000	1.5	9	4.3	1.7	1.2
20	1000	2	3	4.6	1.9	1.3
20	1000	2	4	3.5	1.3	0.9
20	1000	2	5	3.3	1.2	0.8
20	1000	2	7	3.7	1.4	0.9
20	1000	2	9	4.1	1.6	1.1
20	1000	3.5	3	2.1	0.7	0.5
20	1000	3.5	4	2.4	0.8	0.6
20	1000	3.5	5	2.7	1.0	0.7
20	1000	3.5	7	3.4	1.3	0.9
20	1000	3.5	9	4.0	1.5	1.1
30	130	1	3	8.5	4.8	3.6

				Worst Case Estimated Battery Life(Yrs)		
Frequency (Hz)	**Pulse Width (? sec)**	**Output Current (mA)**	**Load Resistance (K?)**	**10% Duty Cycle**	**33% Duty Cycle**	**50% Duty Cycle**
30	130	1	4	8.1	4.4	3.3
30	130	1	5	7.9	4.2	3.1
30	130	1	7	7.9	4.2	3.1
30	130	1	9	7.8	4.1	3.0
30	130	1.5	3	8.4	4.7	3.5
30	130	1.5	4	8.1	4.4	3.3
30	130	1.5	5	8.1	4.4	3.3
30	130	1.5	7	7.1	3.5	2.6
30	130	1.5	9	7.1	3.5	2.6
30	130	2	3	7.9	4.2	3.1
30	130	2	4	7.2	3.6	2.6
30	130	2	5	6.4	3.0	2.1
30	130	2	7	6.5	3.0	2.2
30	130	2	9	6.8	3.2	2.3
30	130	3.5	3	5.6	2.4	1.7
30	130	3.5	4	5.9	2.6	1.8
30	130	3.5	5	6.1	2.8	2.0
30	130	3.5	7	6.5	3.1	2.2
30	130	3.5	9	6.7	3.2	2.3
30	500	1	3	7.4	3.7	2.7
30	500	1	4	6.0	2.7	1.9

				Worst Case Estimated Battery Life(Yrs)		
Frequency (Hz)	**Pulse Width (? sec)**	**Output Current (mA)**	**Load Resistance (K?)**	**10% Duty Cycle**	**33% Duty Cycle**	**50% Duty Cycle**
30	500	1	5	6.7	3.2	2.3
30	500	1	7	5.8	2.5	1.8
30	500	1	9	4.9	2.0	1.4
30	500	1.5	3	6.2	2.8	2.0
30	500	1.5	4	5.7	2.5	1.8
30	500	1.5	5	5.3	2.3	1.6
30	500	1.5	7	4.6	1.8	1.3
30	500	1.5	9	4.7	1.9	1.3
30	500	2	3	5.0	2.1	1.5
30	500	2	4	4.0	1.6	1.1
30	500	2	5	3.8	1.5	1.0
30	500	2	7	4.2	1.6	1.1
30	500	2	9	4.5	1.8	1.2
30	500	3.5	3	2.8	1.0	0.7
30	500	3.5	4	3.1	1.1	0.8
30	500	3.5	5	3.5	1.3	0.9
30	500	3.5	7	2.2	0.7	0.5
30	500	3.5	9	4.5	1.8	1.3
30	1000	1	3	6.2	2.8	2.0
30	1000	1	4	5.0	2.1	1.5

				Worst Case Estimated Battery Life(Yrs)		
Frequency (Hz)	**Pulse Width (? sec)**	**Output Current (mA)**	**Load Resistance (K?)**	**10% Duty Cycle**	**33% Duty Cycle**	**50% Duty Cycle**
30	1000	1	5	5.6	2.5	1.7
30	1000	1	7	4.6	1.8	1.3
30	1000	1	9	3.4	1.3	0.9
30	1000	1.5	3	2.9	1.0	0.7
30	1000	1.5	4	4.1	1.6	1.1
30	1000	1.5	5	3.6	1.3	0.9
30	1000	1.5	7	2.9	1.0	0.7
30	1000	1.5	9	3.2	1.2	0.8
30	1000	2	3	3.5	1.3	0.9
30	1000	2	4	2.7	0.9	0.6
30	1000	2	5	2.3	0.8	0.5
30	1000	2	7	2.8	1.0	0.7
30	1000	2	9	3.1	1.1	0.8
30	1000	3.5	3	1.4	0.5	0.3
30	1000	3.5	4	1.3	0.4	0.3
30	1000	3.5	5	2.0	0.7	0.5
30	1000	3.5	7	2.6	0.9	0.6
30	1000	3.5	9	3.0	1.1	0.7

The projected battery life decreases as Lead impedance increases. Although 1.5 k to 3 k ohms (DC-DC Converter Code 1-2) appears to be the typical Lead impedance at time of implantation, the impedance may increase to 3 k to 5 k ohms (DC-DC Converter Code 2-3) during the life of the implant.

12.1.2.7.1. Pulse Generator Replacement

All VNS Therapy Pulse Generators will eventually require surgical replacement due to battery depletion. Pulse Generator replacement does not, of itself, require Lead replacement unless a Lead fracture is suspected. Pulse Generator replacement or removal requires dissection to the Pulse Generator's pocket, with care being taken not to damage or cut the Lead. Pulse Generator removal is the reverse of the placement procedure. The entire surgical procedure is generally short, about one hour.

12.1.2.8.Lead Lifetime and Replacement

The Lead's lifetime is undetermined at this time. A Lead would require replacement if a Lead fracture were suspected, accompanied by an increase in seizure frequency. Events that can shorten the life expectancy of the Lead are as follows:

- Blunt trauma to the neck and/or any area of the body beneath which the Lead is implanted
- Patient's twisting or picking at either the implanted Lead or the Pulse Generator
- Improper surgical implantation of the VNS Therapy System, including (but not limited to) providing an inadequate strain relief loop, placing sutures directly on the Lead body, not using the tie-downs, and suturing to muscle

⚠ **Lead replacement or removal because of lack of efficacy** is a medical judgement based on the patient's desires and health status, and must be carefully weighed against the known and unknown risks of surgery. At present, there are no known long-term hazards or risks associated with leaving the Lead implanted, beyond those already mentioned in this manual.

12.1.3. Implantation

12.1.3.1.Sterilization, Storage and Handling

⚠ Do not open the package if it has been exposed to **extreme temperatures** or if there is any indication of **external damage** or damage to the package seal. Instead, return it unopened to Cyberonics.

⚠ **Return explanted Pulse Generators** to Cyberonics for examination and proper disposal, along with a completed Returned Product Report form. Before returning the Pulse Generator, disinfect the device components with Betadine®, Cidex® soak, or another similar disinfectant, and double-seal them in a pouch or other container properly labeled with a biohazard warning.

12.1.3.2.Package Contents

The sterile package contains the following:

? ? 1 Cyberonics VNS Therapy Pulse, Model 102 Generator or VNS Therapy Pulse Duo, Model 102R Generator

? ? 1 hex screwdriver

? ? 1 resistor assembly

Also provided along with the sterile package are the following:

? ? 1 Physician's Manual for the VNS Therapy Pulse, Model 102 Generator and VNS Therapy Pulse Duo, Model 102R Generator

? ? 1 Returned Product Form

? ? 8 Product Identification Labels

? ? 1 Implant Warranty and Registration Card

12.1.3.3 Opening the Sterile Package

Before the package is opened, it should be examined carefully for evidence of damage or compromised sterility. If the outer or inner package has been opened or damaged, Cyberonics cannot guarantee sterility of the Pulse Generator, and it should not be used. An opened or damaged product should be returned to Cyberonics.

To open the package, do the following:

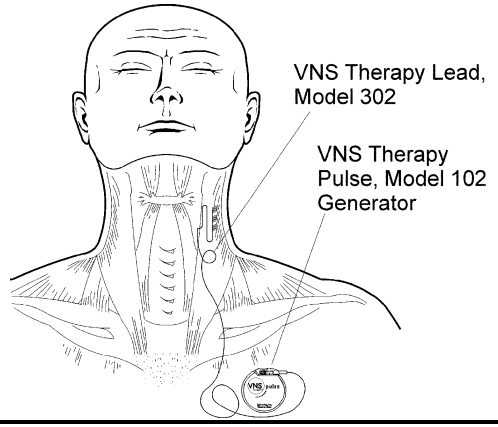
1. Grasp the tab, and peel back the outer cover.
2. Observing sterile technique, lift out the sterile inner tray.
3. Grasp the inner tray's tab, and carefully peel off the inner cover to expose the contents without dropping them.

12.1.3.4 Lead and Pocket Location

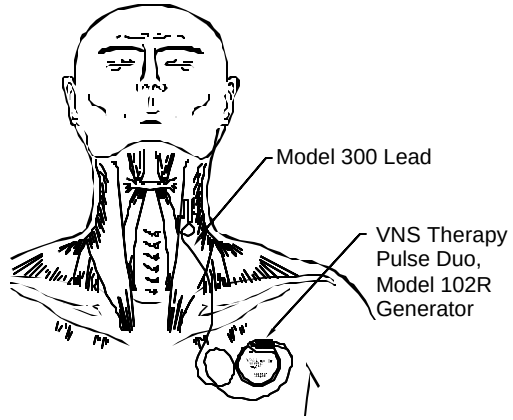
The Pulse Generator is usually implanted just below the clavicle in a subcutaneous pocket in the left upper chest. Suggested placement for the Lead is the area of the left vagus nerve just above the clavicle, with the Lead subcutaneously tunneled between the stimulation site in the neck and the pocket formed in the upper chest (see Figure 10). It is recommended that both the Lead body and the Pulse Generator be positioned on the left side of the body. The Cyberonics VNS Therapy Tunneler is recommended for subcutaneous routing of the Lead.

Figure 10. Placement of Pulse Generator and Lead

Model 102



Model 102R



12.1.3.5.Recommendations for Implantation

In general, implantation of the Pulse Generator and Lead is similar to accepted practice for implantation of a cardiac pacemaker, with the exception of the placement of the electrodes and the subcutaneous routing of the Lead body. Although the surgical approach and techniques will vary with the preference of the implanting physician, to ensure correct Lead placement, the Lead Physician's Manual provides recommendations for implantation, along with a detailed description of the order of placement of the helical electrodes and the anchor tether and other essential steps.

Critical to the long-term success of the implant are proper techniques both for the attachment of the electrodes and the anchor tether to the left vagus nerve, and for the provision of adequate strain relief below and above the sternocleidomastoid muscle.

⚠ **The Lead and its electrodes are very delicate,** and care should be taken not to over stretch or crush the helices.

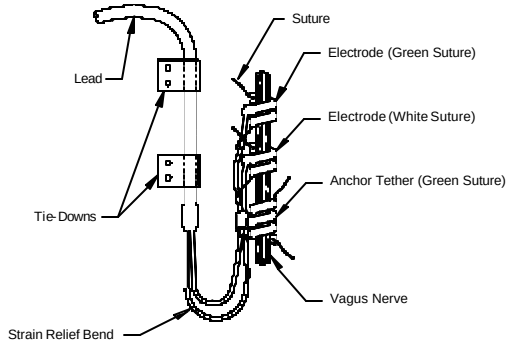
It is recommended that the Lead body be coiled and placed in the chest pocket to the side of the Pulse Generator.

Adequate exposure of the vagus nerve (? 3 cm) facilitates placement of the electrodes on the nerve. Stretching the nerve or allowing it to dry during implantation may result in temporary swelling of the nerve. Constriction of the nerve or other nerve damage may result in vocal cord dysfunction.

⚠ Sutures that are part of the Lead coil are meant to assist in electrode placement around the left vagus nerve.

These sutures should *not* be tied to each other since this may cause nerve damage (see Figure 11).

Figure 11. Use of Tie-downs in Electrode Placement



Cyberonics recommends that output of the Pulse Generator and performance of the implanted system be tested at the time of implantation (see the section on "VNS Therapy System Testing" in this manual). Although an oscilloscope can be used for measurements, Cyberonics recommends use of the appropriate version of the Software and Programming Wand (placed in a sterile drape) for routine system verification.

After the electrode is placed on the nerve, the electrode-nerve interface impedance is tested by connecting the Lead directly to the Pulse Generator and performing a Lead Test. The Pulse Generator is packaged with a separate resistor assembly to be used while performing the optional pre-implant diagnostics.

12.1.3.6.Beginning the Implantation Procedure

To implant the Pulse Generator and Lead, do the following:

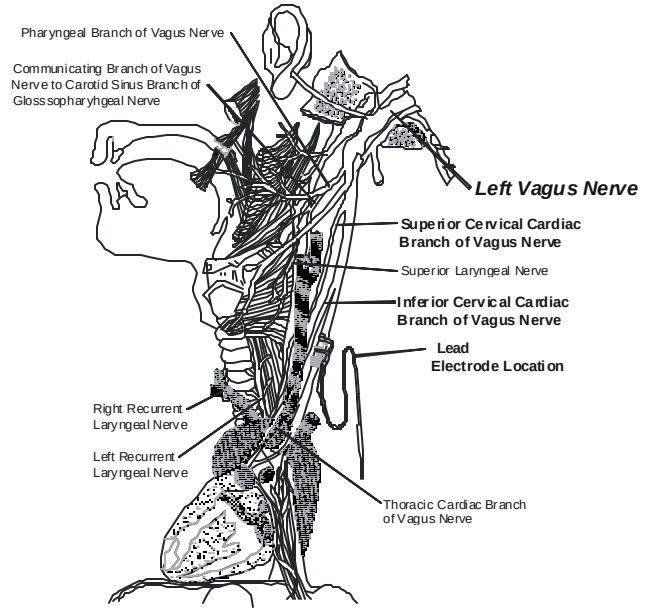
1. After examining the exposed nerve, select an appropriately sized Lead (2.0 or 3.0 mm). The Model 300 or 302-20 (2.0 mm) should accommodate most vagus nerves.

   ⚠ The VNS Therapy Lead is available in two sizes: 2.0 mm and 3.0 mm. Since it is not possible to predict in patients what size Lead will be needed, **Cyberonics recommends that both Lead sizes (2.0 and 3.0 mm) be available in the Operating Room (OR)**. In addition, backups for leads should be available in the event of a sterility compromise or damage induced during surgery.

2. Using the Tunneler, tunnel the connector and Lead body subcutaneously from the neck incision to the Pulse Generator pocket. (For details, see the VNS Therapy Tunneler, Model 402 Directions for Use.)
3. Attach the Lead electrodes to the desired site on the left vagus nerve, securing the electrode body parallel to the nerve using the anchor tether and tie-downs. (See the VNS Therapy Lead Physician's Manual for more detailed instructions.)

It is very important that the surgeon implanting the VNS Therapy System be familiar with vagus nerve anatomy, particularly the cardiac branches. The Lead electrodes must not be placed on either the superior or the inferior cervical cardiac branches. **Place them below where the superior and inferior cervical cardiac branches separate from the vagus nerve.** Stimulation of either of these two branches during the Lead Test may cause **bradycardia and/ asystole.** Careful dissection laterally on the vagus nerve should aid the physician in determining proper electrode placement. In most but not all patients, the main vagus nerve is the largest of the three nerves. Figure 12 shows the correct anatomical placement of the electrodes.

Figure 12. Vagus Nerve Anatomy and Placement of the Lead



⚠ Attachment of Lead electrodes must not involve the superior cervical cardiac branch or the inferior cervical cardiac branch of the vagus nerve. Place the electrodes *below* where these two branches separate from the vagus nerve.

⚠ Excessive manipulation of the vagus nerve during placement of the Lead can result in noticeable postoperative hoarseness. Under most circumstances, this condition will resolve without additional medical intervention within three to four weeks, depending on the degree of stress applied to the nerve during surgery. Cyberonics does not recommend that stimulation treatment be initiated until this condition has resolved, since it could worsen the condition.

⚠ In the procedures below, ensure that the hex screwdriver is fully inserted in the setscrew, and then push in on the hex screwdriver and turn it clockwise until it clicks. To avoid damaging (stripping) the setscrew(s) and/or dislodging the setscrew plug(s), insert the hex screwdriver into the center of the setscrew plug, keeping the hex screwdriver perpendicular to the Pulse Generator.

⚠ When using the hex screwdriver grasp it by the handle only, as shown in Figure 14. Do not grasp any other portion of the hex screwdriver during use as this may affect its proper function.

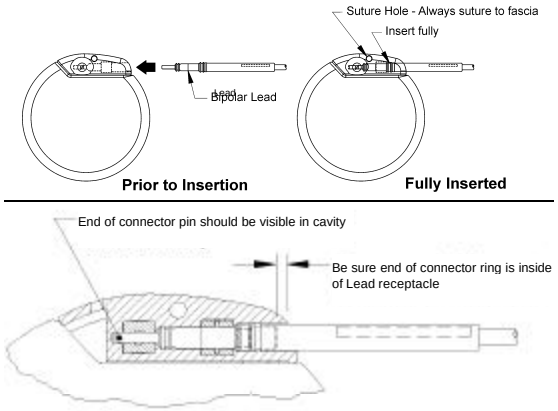
4. Connect the Lead directly to the Pulse Generator:

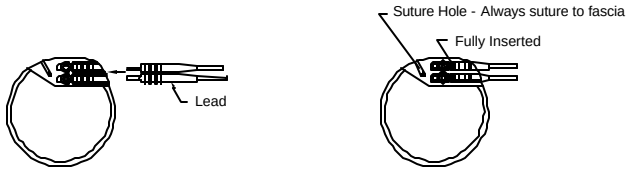
   ✍✍ Verify by looking inside the Pulse Generator Lead receptacle(s) that the setscrew(s) has been adequately backed out to allow full insertion of the connector pin(s). Avoid backing the setscrew(s) out further than needed for Lead insertion.

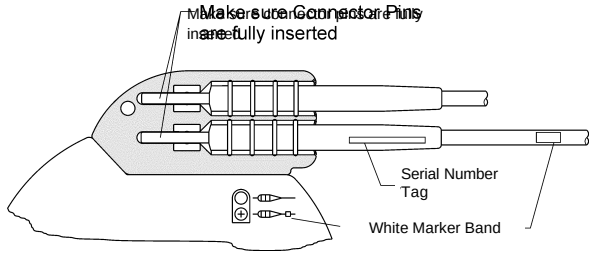
   ✍✍ Insert the hex screwdriver through the center of the setscrew plug(s) to vent back pressure built up during Lead insertion.

Figure 13. Lead Connector(s) Prior to Insertion and Fully Inserted

Model 102







✍✍When using a Model 102 Generator and Model 302 Lead, insert the Lead connector pin fully into the Pulse Generator header. To allow escape of the back pressure created by insertion, leave the tip of the hex screwdriver in the slit in the setscrew plug.

✍✍When using a Model 102R Generator and Model 300 Lead, insert the Lead connector pins fully into the appropriate Lead receptacles in the Pulse Generator header. To allow escape of the back pressure created by insertion, leave the tip of the hex screwdriver in the slit in the setscrew plug of the connector being inserted. Insert the lead connector with the white marker band and with the embedded model number and serial number tag into the Lead receptacle labeled “+”(see Model 102R figure above). The remaining Lead connector is inserted into the remaining Lead receptacle.

✍✍With the hex screwdriver still inserted through the setscrew plug, verify that the connector pin is fully inserted. The pin should be visible in the area at the back end of the setscrew connector block. If it is not, remove the pin. To loosen the setscrew, engage the hex screwdriver into the setscrew, and turn it counterclockwise until the connector pin can be fully inserted. Avoid backing the setscrew out further than needed for Lead insertion. If using the Model 102R, repeat this procedure for each setscrew.

✍✍ After verifying that the connector pin(s) has been fully inserted, tighten each setscrew by engaging the setscrew with the hex screwdriver and turning the hex screwdriver clockwise until it begins to click. Always push in on the hex screwdriver while turning it to ensure that the hex screwdriver is fully inserted in the setscrew.

⚠ **It is important to do the following:**

- ✍✍ Carefully insert the Lead connector pin(s) into the Lead receptacle(s) without bending the Lead connector(s).
- ✍✍ Visually inspect that the connector pin(s) is clean and completely inserted.
- ✍✍ Ensure that the Lead receptacle(s) is clean and free of obstruction.

Electrical connection to the Pulse Generator is not established until the setscrew(s) is completely tightened with the hex screwdriver. Failure to make a good connection can result in a Lead Test failure or erratic stimulation at varying intensity due to rapid, unpredictable changes in Lead impedance, which is expected to adversely affect device effectiveness and may have serious safety consequences.

✍✍ Gently pull on Lead connector boot(s) (thick section) to verify Lead is properly secured inside the Lead receptacle(s). Do not pull on Lead body (thin section) or use excessive pull force because doing so may cause Lead damage.

⚠ **Reversal of Lead polarity has been associated with an increased chance of bradycardia** in animal studies. It is important to make sure that the Lead connector pins in the Model 300 Lead are correctly inserted (white marker band to + connection) into the Model 102R Pulse Generator Lead receptacles.

5. Test the Pulse Generator and Lead (see the section "VNS Therapy System Testing" in this manual) before completing the implantation procedure. If tests for both components are successful, the implantation procedure can continue.

12.1.3.7.VNS Therapy System Testing

The Lead Test, which should be conducted first, is performed with the Lead and the Pulse Generator connected. Thus, if the Lead Test is successful, both components are working properly. However, if the Lead Test fails, either of the two components could be defective, or there may not be a good electrical connection between the Pulse Generator and the Lead connector pin(s). If a defective component is suspected, disconnect the Lead and perform the optional Pulse Generator (Pre-Implant) Test using the resistor assembly supplied with the Pulse Generator.

⚠ During the intraoperative Lead Test, rare incidents of **bradycardia and/or asystole** have occurred. As of October 1998, approximately 3,000 patients had been implanted with the VNS Therapy System. Four of these patients were reported to have experienced bradycardia and/or asystole during the intraoperative Lead Test. All four patients recovered without sequelae. One of the four patients was implanted with the VNS Therapy System. There were no postoperative or VNS Therapy System treatment-related cardiac adverse events later reported for that patient. No similar events were reported to have occurred during the clinical studies at the time of implantation or during treatment.

The safety of this therapy has not been systematically established for patients experiencing bradycardia or asystole during VNS Therapy System implantation.

Lead Test

To test the Lead (the impedance of the electrode-nerve interface), do the following:

1. Verify that the Lead impedance status is "OK" (for details, see the Model 250 Software Physician's Manual).
2. If Lead impedance status is not "OK", verify that the Lead connector pin(s) is properly inserted into the Lead receptacles and that the setscrew is tightened.
3. Repeat the Lead Test. If the test fails again (the status check is "HIGH"), the problem is with *either* the Lead *or* the Pulse Generator.

A test of the Pulse Generator will determine the source of the problem.

Pulse Generator Test (“Pre-implant Test”)

If the Lead Test fails twice, then the Pulse Generator Test (“Pre-implant Test”) is necessary to determine whether the Lead or the Pulse Generator is the problem. A successful Pulse Generator Test will confirm that the Lead (not the Pulse Generator) is defective; a failed Pulse Generator Test will confirm that the Pulse Generator is defective.

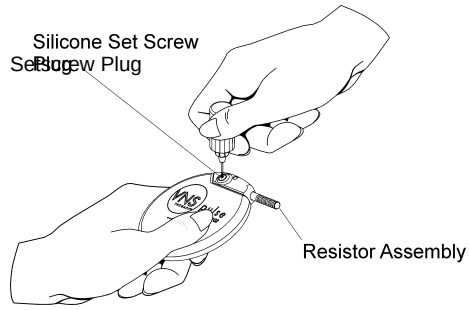
To test the Pulse Generator (“Pre-implant Test”), do the following:

1. Remove the Lead connector pin(s) from the Lead receptacles. Removal is accomplished by inserting the hex screwdriver through the center of the setscrew plug(s) and loosening the setscrew(s). Avoid backing the setscrew(s) out more than necessary to remove the Lead. No more than a half turn should be necessary to remove the Lead.
2. Insert the connector pin(s) of the resistor assembly into the Lead receptacle(s). Take care while inserting the test resistor pin(s) into the Lead receptacle(s). If binding or significant resistance is felt, remove the test resistor. Without the use of excessive force, reinsert the test resistor.

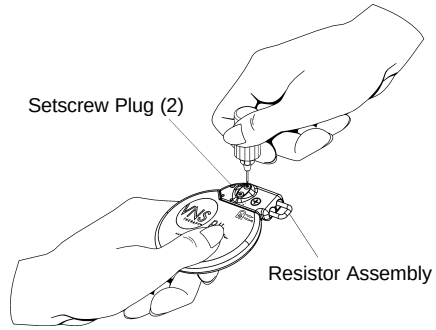
   Note: Fully insert the hex screwdriver into the setscrew and push in on the hex screwdriver whenever the setscrew(s) is being tightened or loosened.
3. When the resistor assembly is in place, tighten the setscrew(s) until the hex screwdriver begins to click (see Figure 14). Again, always push in on the hex screwdriver while turning it to ensure that the hex screwdriver is fully inserted in the setscrew.

Figure 14. Connecting the Resistor Assembly

Model 102



Model 102R



4. Perform the Pulse Generator Test (for details, see the Model 250 Software Physician's Manual).

If the Pulse Generator Test ("Pre-implant Test") is successful ("OK"), it is safe to assume that the Lead is defective. However, if the test fails (the status reads "HIGH"), it is the Pulse Generator that is defective.

If either component is defective or damaged, contact Cyberonics and return the item (following the disinfection procedure described in the “Precautions” section of this manual), along with a completed Returned Product Report.

Optional Monitoring

Optional physiologic monitoring of VNS Therapy System operation may be done if surgery is performed under local anesthesia. Monitor the patient’s voice for signs of hoarseness while gradually increasing the Pulse Generator output current. After testing, reset the current to 0 mA.

12.1.3.8.Completing the Implantation Procedure

After the testing has been completed, finish the implantation procedure:

1. Place the Pulse Generator in the chest pocket, coiling the remaining slack of the Lead and placing it to the side of the Pulse Generator. The Pulse Generator can be placed with either side facing outward.

   ⚠ Do not place the Lead slack under the Pulse Generator, because doing so could result in insulation failure and system malfunction.

2. Secure the Pulse Generator by placing a suture through the suture hole.

   ⚠ This suturing is important to stabilize the Pulse Generator and to prevent manipulation by the patient, which could damage the Lead wires.

   ⚠ Do not place the sutures directly around the body of the Lead; this could result in insulation failure

and system malfunction, and possible Lead breakage.

3. Close the surgical incisions. Use cosmetic closure techniques to minimize scarring.

A neck brace can be used by the patient for the first week to help ensure proper Lead stabilization.

12.1.4. Follow-up Information

12.1.4.1.Guidelines for Patient Follow Up

During the first few weeks after implantation, the patient should be seen to confirm wound healing and proper Pulse Generator operation. The Pulse Generator's output current for both the magnet and the programmed stimulation must be 0.0 mA for the first 14 days after implantation.

The VNS Therapy System is an adjunctive therapy to existing (prior to device implantation) antiepileptic medications. Cyberonics strongly encourages physicians **to keep all antiepileptic medications stable for the first three months** of stimulation before attempting to reduce or change a patient's medication.

During initial programming, the output current should be programmed to start at nominal parameters (0 mA) and then be slowly increased in 0.25 mA increments until the patient feels the stimulation at a comfortable level. Patients who are receiving replacement generators should also be started at nominal parameters, with 0.25 mA-step increases to allow re-accommodation.

Cyberonics recommends that testing of the magnet output be performed while the patient is still in the physician's office to ensure tolerability of the magnet output. The magnet output should be programmed at each visit, if necessary, to a level that is perceptible to the patient.

Some patients have reported that it is easier to verify daily that stimulation is being delivered if the magnet output current is set to one step above normal stimulation settings. This slightly higher output current is intended to allow patients who have accommodated to normal stimulation to recognize or perceive the magnet stimulation, thereby confirming device function.

At each patient visit, the Pulse Generator should be interrogated using the appropriate version of the VNS Therapy Software. After reprogramming and/or diagnostics testing, data should be printed out and filed (see the Model 250 VNS Therapy Software Physician's Manual for instructions on printing out data). These data can be used for comparison with a patient's diary or own records to evaluate the VNS Therapy System, to confirm proper VNS Therapy System functioning, and to assess the need for reprogramming.

The average output current used during the clinical studies was about 1.0 mA. Other standard treatment settings were 30 Hz, 500 ?sec pulse width, 30 sec ON time, and five min OFF time. There are no data to verify that these are optimal parameters.

There is no proven correlation at present between high output current (m Amps) and device effectiveness, nor is there a standard treatment level that needs to be achieved during treatment ramping. VNS Therapy System treatment should not be uncomfortable, nor should it cause bothersome side effects. Patients should be observed for at least 30 minutes after the last stimulation adjustment to make certain that they are comfortable with both magnet-activated and programmed stimulation.

Although Cyberonics recommends adjusting output current as necessary, there are no controlled data at this time to indicate that higher current levels are associated with better efficacy. Patients whose seizures are well controlled at follow up should not have their settings changed unless they experience uncomfortable side effects.

The subsequent follow-up schedule and the nature of each examination should be determined by the physician on the basis of patient response to and tolerance of the implant. In all other respects, follow up should be performed in accordance with the standard medical practice for patients with epilepsy.

12.1.4.2.Patient Identification

Included with the Pulse Generator is an Implant Warranty and Registration Card that *must* be completed and the top, white copy returned to Cyberonics. This information, as required by government agencies, becomes part of the Cyberonics' registry of implantees and is used as a permanent record of implant recipient information. In addition to the form, a wallet-sized Patient Emergency Information Card is enclosed that contains information about the Pulse Generator. The patient should be instructed to carry this card at all times.

12.1.4.3.End-of-Service and Replacement Information

Cyberonics recommends that patients be instructed to activate the Pulse Generator manually with a magnet on a daily basis to test for the presence of stimulation. The most common reason for the absence of stimulation is battery depletion, though there may be other reasons. The magnet output current should be programmed to a level that is perceptible to the patient. Patients must be instructed to call their physician when they notice that magnet-activated stimulation is no longer perceptible.

The lifetime of the Pulse Generator battery depends on programmed parameters and Lead impedance (see Tables 12 and 13). Immediately before end of service (EOS), the Pulse Generator may provide unscheduled stimulation. The stimulation output may be above or below the programmed output. When EOS occurs, the Pulse Generator will not deliver any output, the patient will not feel the stimulation, and communication with the Pulse Generator will not be possible.

⚠ Pulse Generator EOS may result in increased seizure frequency and/or seizure intensity and/or seizure duration, in some cases to levels greater than those reported before stimulation.

Model 102 and Model 102R Pulse Generators have an elective replacement indicator (ERI) that provides a warning period prior to EOS. The time from ERI to EOS is highly dependent on the programmed parameters and the Lead impedance. Tables 14 and 15 provide estimated times from ERI to EOS under a variety of stimulation conditions, including Lead impedance. Because of the number of possible parameter combinations, it is impractical to provide the estimated times for all possible combinations.

Once ERI is detected, immediate replacement is recommended.

Table 14. Estimated Battery Life - Nominal ERI to EOS Time Estimates

				Nominal Time from ERI to EOS (Months)		
Frequency (Hz)	Pulse Width (? sec)	Output Current (mA)	Load Resistance (K?)	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
10	130	1	3	22.0	16.5	13.9
10	130	1	4	21.7	16.0	13.4
10	130	1	5	20.7	14.4	11.7
10	130	1	7	19.7	12.9	10.2
10	130	1	9	18.4	11.2	8.7
10	130	1.5	3	20.2	13.5	10.8
10	130	1.5	4	19.7	12.9	10.2
10	130	1.5	5	19.1	12.0	9.4
10	130	1.5	7	17.7	10.3	7.9
10	130	1.5	9	17.7	10.3	7.9
10	130	2	3	19.5	12.6	10.0
10	130	2	4	18.7	11.5	9.0
10	130	2	5	17.3	9.9	7.5
10	130	2	7	17.6	10.2	7.7
10	130	2	9	17.9	10.5	8.1
10	130	3.5	3	16.2	8.7	6.5
10	130	3.5	4	16.4	8.9	6.7
10	130	3.5	5	16.7	9.2	6.9
10	130	3.5	7	17.4	10.0	7.6

				Nominal Time from ERI to EOS (Months)		
Frequency (Hz)	Pulse Width (? sec)	Output Current (mA)	Load Resistance (K?)	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
10	130	3.5	9	17.9	10.5	8.1
10	500	1	3	19.7	12.9	10.2
10	500	1	4	19.4	12.4	9.8
10	500	1	5	18.5	11.3	8.8
10	500	1	7	17.0	9.5	7.2
10	500	1	9	15.9	8.5	6.3
10	500	1.5	3	17.6	10.2	7.7
10	500	1.5	4	16.4	9.0	6.8
10	500	1.5	5	15.3	8.0	5.9
10	500	1.5	7	13.6	6.5	4.7
10	500	1.5	9	14.3	7.1	5.1
10	500	2	3	15.5	8.1	6.0
10	500	2	4	14.3	7.1	5.2
10	500	2	5	12.6	5.8	4.1
10	500	2	7	13.1	6.1	4.4
10	500	2	9	14.0	6.8	5.0
10	500	3.5	3	9.9	4.1	2.9
10	500	3.5	4	10.5	4.5	3.1
10	500	3.5	5	11.3	5.0	3.5
10	500	3.5	7	12.4	5.7	4.0
10	500	3.5	9	13.3	6.3	4.6

				Nominal Time from ERI to EOS (Months)		
Frequency (Hz)	Pulse Width (? sec)	Output Current (mA)	Load Resistance (K?)	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
10	1000	1	3	17.0	9.5	7.2
10	1000	1	4	16.9	9.5	7.1
10	1000	1	5	15.7	8.3	6.2
10	1000	1	7	13.7	6.6	4.8
10	1000	1	9	12.7	5.9	4.2
10	1000	1.5	3	14.4	7.2	5.3
10	1000	1.5	4	13.4	6.4	4.6
10	1000	1.5	5	12.1	5.5	3.9
10	1000	1.5	7	10.5	4.4	3.1
10	1000	1.5	9	11.0	4.7	3.3
10	1000	2	3	12.2	5.5	4.0
10	1000	2	4	10.3	4.4	3.0
10	1000	2	5	9.1	3.7	2.5
10	1000	2	7	9.7	4.0	2.8
10	1000	2	9	10.6	4.5	3.2
10	1000	3.5	3	6.3	2.3	1.6
10	1000	3.5	4	7.0	2.6	1.8
10	1000	3.5	5	7.9	3.0	2.1
10	1000	3.5	7	9.2	3.7	2.6
10	1000	3.5	9	10.1	4.2	2.9
20	130	1	3	20.5	14.0	11.3

				Nominal Time from ERI to EOS (Months)		
Frequency (Hz)	Pulse Width (? sec)	Output Current (mA)	Load Resistance (K?)	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
20	130	1	4	19.6	12.7	10.1
20	130	1	5	18.8	11.6	9.1
20	130	1	7	17.4	10.0	7.6
20	130	1	9	16.2	8.8	6.6
20	130	1.5	3	18.0	10.6	8.2
20	130	1.5	4	17.1	9.7	7.4
20	130	1.5	5	16.2	8.8	6.6
20	130	1.5	7	14.7	7.4	5.4
20	130	1.5	9	14.9	7.6	5.6
20	130	2	3	16.8	9.4	7.1
20	130	2	4	15.6	8.2	6.1
20	130	2	5	14.2	7.0	5.1
20	130	2	7	14.6	7.3	5.4
20	130	2	9	15.1	7.8	5.7
20	130	3.5	3	12.5	5.7	4.1
20	130	3.5	4	12.8	6.0	4.3
20	130	3.5	5	13.3	6.3	4.6
20	130	3.5	7	14.1	6.9	5.0
20	130	3.5	9	14.8	7.5	5.5
20	500	1	3	16.7	9.2	6.9
20	500	1	4	16.4	8.9	6.7

				Nominal Time from ERI to EOS (Months)		
Frequency (Hz)	Pulse Width (? sec)	Output Current (mA)	Load Resistance (K?)	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
20	500	1	5	14.5	7.3	5.3
20	500	1	7	13.4	6.4	4.6
20	500	1	9	12.4	5.6	4.0
20	500	1.5	3	14.0	6.8	5.0
20	500	1.5	4	12.8	5.9	4.3
20	500	1.5	5	11.7	5.2	3.7
20	500	1.5	7	10.0	4.2	2.9
20	500	1.5	9	10.6	4.5	3.2
20	500	2	3	11.8	5.3	3.8
20	500	2	4	10.5	4.4	3.1
20	500	2	5	8.9	3.6	2.5
20	500	2	7	9.6	3.9	2.7
20	500	2	9	10.4	4.4	3.1
20	500	3.5	3	6.5	2.4	1.6
20	500	3.5	4	7.1	2.6	1.8
20	500	3.5	5	7.9	3.1	2.1
20	500	3.5	7	9.1	3.7	2.5
20	500	3.5	9	9.9	4.1	2.9
20	1000	1	3	12.7	5.8	4.2
20	1000	1	4	13.3	6.3	4.6
20	1000	1	5	12.2	5.5	4.0

				Nominal Time from ERI to EOS (Months)		
Frequency (Hz)	Pulse Width (? sec)	Output Current (mA)	Load Resistance (K?)	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
20	1000	1	7	10.2	4.3	3.0
20	1000	1	9	8.9	3.5	2.4
20	1000	1.5	3	10.6	4.5	3.2
20	1000	1.5	4	9.5	3.9	2.7
20	1000	1.5	5	8.5	3.3	2.3
20	1000	1.5	7	6.8	2.5	1.7
20	1000	1.5	9	7.4	2.8	1.9
20	1000	2	3	8.2	3.2	2.2
20	1000	2	4	6.4	2.3	1.6
20	1000	2	5	5.7	2.1	1.4
20	1000	2	7	6.4	2.3	1.6
20	1000	2	9	7.2	2.7	1.9
20	1000	3.5	3	3.7	1.3	0.8
20	1000	3.5	4	4.3	1.5	1.0
20	1000	3.5	5	4.9	1.7	1.2
20	1000	3.5	7	5.9	2.1	1.5
20	1000	3.5	9	6.7	2.5	1.7
30	130	1	3	19.3	12.3	9.7
30	130	1	4	18.6	11.4	8.9
30	130	1	5	17.1	9.7	7.4
30	130	1	7	15.7	8.3	6.1

				Nominal Time from ERI to EOS (Months)		
Frequency (Hz)	Pulse Width (? sec)	Output Current (mA)	Load Resistance (K?)	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
30	130	1	9	14.6	7.3	5.4
30	130	1.5	3	16.4	8.9	6.7
30	130	1.5	4	15.5	8.1	6.0
30	130	1.5	5	14.7	7.4	5.4
30	130	1.5	7	13.0	6.1	4.4
30	130	1.5	9	13.3	6.3	4.5
30	130	2	3	14.9	7.6	5.6
30	130	2	4	13.8	6.7	4.9
30	130	2	5	12.1	5.5	3.9
30	130	2	7	12.5	5.7	4.1
30	130	2	9	13.0	6.1	4.4
30	130	3.5	3	10.2	4.3	3.0
30	130	3.5	4	10.7	4.5	3.2
30	130	3.5	5	11.2	4.9	3.5
30	130	3.5	7	12.0	5.4	3.8
30	130	3.5	9	12.6	5.8	4.1
30	500	1	3	14.1	6.9	5.0
30	500	1	4	13.7	6.6	4.8
30	500	1	5	13.0	6.1	4.4
30	500	1	7	11.1	4.8	3.4
30	500	1	9	9.9	4.1	2.9

				Nominal Time from ERI to EOS (Months)		
Frequency (Hz)	Pulse Width (? sec)	Output Current (mA)	Load Resistance (K?)	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
30	500	1.5	3	11.6	5.2	3.7
30	500	1.5	4	10.6	4.5	3.2
30	500	1.5	5	9.6	3.9	2.7
30	500	1.5	7	7.9	3.1	2.1
30	500	1.5	9	8.5	3.4	2.3
30	500	2	3	9.4	3.8	2.7
30	500	2	4	8.0	3.1	2.1
30	500	2	5	6.8	2.5	1.7
30	500	2	7	7.4	2.8	1.9
30	500	2	9	8.3	3.2	2.2
30	500	3.5	3	4.8	1.7	1.1
30	500	3.5	4	5.3	1.9	1.3
30	500	3.5	5	6.0	2.2	1.5
30	500	3.5	7	7.8	3.0	2.1
30	500	3.5	9	8.0	3.1	2.1
30	1000	1	3	11.2	4.9	3.4
30	1000	1	4	10.4	4.4	3.1
30	1000	1	5	10.0	4.1	2.9
30	1000	1	7	8.0	3.1	2.1
30	1000	1	9	6.6	2.5	1.7
30	1000	1.5	3	7.8	3.0	2.1

				Nominal Time from ERI to EOS (Months)		
Frequency (Hz)	Pulse Width (? sec)	Output Current (mA)	Load Resistance (K?)	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
30	1000	1.5	4	7.1	2.7	1.8
30	1000	1.5	5	6.3	2.3	1.6
30	1000	1.5	7	5.1	1.8	1.2
30	1000	1.5	9	5.7	2.0	1.4
30	1000	2	3	6.0	2.2	1.5
30	1000	2	4	4.7	1.6	1.1
30	1000	2	5	4.2	1.4	1.0
30	1000	2	7	4.8	1.7	1.1
30	1000	2	9	5.5	1.9	1.3
30	1000	3.5	3	2.6	0.9	0.6
30	1000	3.5	4	3.2	1.1	0.7
30	1000	3.5	5	3.5	1.2	0.8
30	1000	3.5	7	4.4	1.5	1.0
30	1000	3.5	9	5.1	1.8	1.2

Table 15. Estimated Battery Life - Worst Case ERI to EOS Time Estimates

				Worst Case Time from ERI to EOS (Months)		
Frequency (Hz)	Pulse Width (? sec)	Output Current (mA)	Load Resistance (K?)	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
10	130	1	3	15.5	10.3	8.3
10	130	1	4	15.9	11.0	9.0
10	130	1	5	14.8	9.4	7.4
10	130	1	7	13.7	8.1	6.2
10	130	1	9	12.1	6.4	4.8
10	130	1.5	3	11.5	5.9	4.3
10	130	1.5	4	11.8	6.1	4.5
10	130	1.5	5	12.0	6.3	4.7
10	130	1.5	7	13.7	8.1	6.2
10	130	1.5	9	12.9	7.2	5.4
10	130	2	3	11.6	6.0	4.4
10	130	2	4	9.8	4.5	3.2
10	130	2	5	9.1	4.0	2.9
10	130	2	7	9.7	4.5	3.2
10	130	2	9	9.4	4.2	3.0
10	130	3.5	3	8.4	3.6	2.5
10	130	3.5	4	8.2	3.5	2.5
10	130	3.5	5	9.2	4.1	2.9
10	130	3.5	7	10.4	5.0	3.6
10	130	3.5	9	10.7	5.2	3.8

				Worst Case Time from ERI to EOS (Months)		
Frequency (Hz)	Pulse Width (? sec)	Output Current (mA)	Load Resistance (K?)	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
10	500	1	3	13.0	7.3	5.5
10	500	1	4	13.7	8.1	6.2
10	500	1	5	13.6	8.0	6.1
10	500	1	7	12.4	6.7	5.0
10	500	1	9	11.9	6.2	4.6
10	500	1.5	3	13.7	8.1	6.2
10	500	1.5	4	14.6	9.1	7.1
10	500	1.5	5	13.6	7.9	6.1
10	500	1.5	7	11.4	5.8	4.2
10	500	1.5	9	12.4	6.7	5.0
10	500	2	3	8.0	3.4	2.4
10	500	2	4	8.8	3.9	2.7
10	500	2	5	10.1	4.7	3.4
10	500	2	7	8.8	3.9	2.7
10	500	2	9	7.7	3.2	2.2
10	500	3.5	3	7.8	3.3	2.3
10	500	3.5	4	6.9	2.8	1.9
10	500	3.5	5	6.7	2.6	1.8
10	500	3.5	7	6.9	2.8	1.9
10	500	3.5	9	9.4	4.3	3.0
10	1000	1	3	14.7	9.3	7.3

				Worst Case Time from ERI to EOS (Months)		
Frequency (Hz)	Pulse Width (? sec)	Output Current (mA)	Load Resistance (K?)	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
10	1000	1	4	14.2	8.6	6.7
10	1000	1	5	12.3	6.6	4.9
10	1000	1	7	13.0	7.3	5.5
10	1000	1	9	13.7	8.1	6.2
10	1000	1.5	3	12.2	6.5	4.8
10	1000	1.5	4	11.8	6.2	4.6
10	1000	1.5	5	11.7	6.0	4.4
10	1000	1.5	7	10.3	4.9	3.6
10	1000	1.5	9	10.5	5.1	3.7
10	1000	2	3	11.5	5.9	4.3
10	1000	2	4	11.1	5.5	4.0
10	1000	2	5	8.5	3.7	2.6
10	1000	2	7	9.5	4.3	3.1
10	1000	2	9	11.6	6.0	4.4
10	1000	3.5	3	7.6	3.1	2.2
10	1000	3.5	4	7.1	2.8	2.0
10	1000	3.5	5	6.2	2.4	1.7
10	1000	3.5	7	5.4	2.0	1.4
10	1000	3.5	9	4.8	1.8	1.2
20	130	1	3	14.5	9.1	7.1
20	130	1	4	13.6	7.9	6.0
20	130	1	5	14.3	8.8	6.8

				Worst Case Time from ERI to EOS (Months)		
Frequency (Hz)	Pulse Width (? sec)	Output Current (mA)	Load Resistance (K?)	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
20	130	1	7	12.9	7.2	5.4
20	130	1	9	12.7	7.0	5.2
20	130	1.5	3	1.0	0.3	0.2
20	130	1.5	4	9.9	4.6	3.3
20	130	1.5	5	10.5	5.0	3.6
20	130	1.5	7	11.5	5.8	4.3
20	130	1.5	9	10.5	5.0	3.6
20	130	2	3	8.9	3.9	2.8
20	130	2	4	7.9	3.3	2.3
20	130	2	5	7.9	3.3	2.3
20	130	2	7	7.6	3.1	2.2
20	130	2	9	7.0	2.8	1.9
20	130	3.5	3	8.3	3.8	2.7
20	130	3.5	4	5.3	2.0	1.3
20	130	3.5	5	6.6	2.6	1.8
20	130	3.5	7	7.6	3.2	2.2
20	130	3.5	9	8.1	3.4	2.4
20	500	1	3	13.2	7.5	5.7
20	500	1	4	12.7	7.0	5.2
20	500	1	5	11.7	6.1	4.5
20	500	1	7	10.6	5.1	3.7

				Worst Case Time from ERI to EOS (Months)		
Frequency (Hz)	Pulse Width (? sec)	Output Current (mA)	Load Resistance (K?)	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
20	500	1	9	11.1	5.6	4.1
20	500	1.5	3	12.0	6.3	4.7
20	500	1.5	4	12.7	7.0	5.3
20	500	1.5	5	6.6	2.6	1.8
20	500	1.5	7	8.9	3.9	2.8
20	500	1.5	9	10.4	5.0	3.6
20	500	2	3	5.2	1.9	1.3
20	500	2	4	6.2	2.4	1.7
20	500	2	5	7.7	3.2	2.2
20	500	2	7	7.5	3.1	2.1
20	500	2	9	5.7	2.2	1.5
20	500	3.5	3	5.7	2.2	1.5
20	500	3.5	4	5.0	1.9	1.3
20	500	3.5	5	4.6	1.6	1.1
20	500	3.5	7	4.7	1.7	1.2
20	500	3.5	9	6.5	2.5	1.8
20	1000	1	3	12.6	6.8	5.1
20	1000	1	4	10.0	4.7	3.4
20	1000	1	5	10.1	4.8	3.4
20	1000	1	7	10.6	5.2	3.7
20	1000	1	9	11.4	5.8	4.2
20	1000	1.5	3	10.2	4.8	3.5

				Worst Case Time from ERI to EOS (Months)		
Frequency (Hz)	Pulse Width (? sec)	Output Current (mA)	Load Resistance (K?)	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
20	1000	1.5	4	9.4	4.3	3.1
20	1000	1.5	5	8.3	3.5	2.5
20	1000	1.5	7	7.8	3.3	2.3
20	1000	1.5	9	7.4	3.0	2.1
20	1000	2	3	5.5	2.1	1.4
20	1000	2	4	9.5	4.4	3.1
20	1000	2	5	6.6	2.6	1.8
20	1000	2	7	8.3	3.6	2.5
20	1000	2	9	9.5	4.3	3.1
20	1000	3.5	3	5.5	2.1	1.4
20	1000	3.5	4	4.6	1.7	1.1
20	1000	3.5	5	3.7	1.3	0.9
20	1000	3.5	7	3.3	1.1	0.8
20	1000	3.5	9	2.8	0.9	0.6
30	130	1	3	12.4	6.7	5.0
30	130	1	4	11.8	6.2	4.6
30	130	1	5	11.4	5.8	4.3
30	130	1	7	11.5	5.8	4.3
30	130	1	9	11.3	5.7	4.2
30	130	1.5	3	7.9	3.3	2.3
30	130	1.5	4	8.4	3.6	2.5

				Worst Case Time from ERI to EOS (Months)		
Frequency (Hz)	Pulse Width (? sec)	Output Current (mA)	Load Resistance (K?)	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
30	130	1.5	5	8.8	3.9	2.7
30	130	1.5	7	9.6	4.4	3.2
30	130	1.5	9	9.4	4.2	3.0
30	130	2	3	7.1	2.9	2.0
30	130	2	4	5.6	2.1	1.5
30	130	2	5	6.3	2.5	1.7
30	130	2	7	5.7	2.2	1.5
30	130	2	9	5.3	2.0	1.4
30	130	3.5	3	4.3	1.6	1.1
30	130	3.5	4	4.0	1.4	0.9
30	130	3.5	5	4.9	1.8	1.2
30	130	3.5	7	5.7	2.2	1.5
30	130	3.5	9	4.0	1.4	1.0
30	500	1	3	12.3	6.6	4.9
30	500	1	4	11.8	6.1	4.5
30	500	1	5	11.8	6.2	4.6
30	500	1	7	10.3	4.9	3.5
30	500	1	9	10.3	4.9	3.5
30	500	1.5	3	10.7	5.2	3.8
30	500	1.5	4	8.5	3.7	2.6
30	500	1.5	5	9.6	4.4	3.1
30	500	1.5	9	8.2	3.5	2.5

				Worst Case Time from ERI to EOS (Months)		
Frequency (Hz)	Pulse Width (? sec)	Output Current (mA)	Load Resistance (K?)	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
30	500	1.5	7	6.9	2.8	1.9
30	500	2	3	3.8	1.3	0.9
30	500	2	4	4.9	1.8	1.2
30	500	2	5	6.4	2.5	1.7
30	500	2	7	3.0	1.0	0.7
30	500	2	9	4.2	1.5	1.0
30	500	3.5	3	4.2	1.5	1.0
30	500	3.5	4	3.8	1.3	0.9
30	500	3.5	5	3.1	1.1	0.7
30	500	3.5	7	3.6	1.3	0.9
30	500	3.5	9	4.8	1.8	1.2
30	1000	1	3	11.4	5.8	4.2
30	1000	1	4	10.4	5.0	3.6
30	1000	1	5	9.2	4.1	2.9
30	1000	1	7	9.3	4.2	3.0
30	1000	1	9	9.7	4.5	3.2
30	1000	1.5	3	8.9	3.9	2.8
30	1000	1.5	4	8.2	3.5	2.4

				Worst Case Time from ERI to EOS (Months)		
Frequency (Hz)	Pulse Width (? sec)	Output Current (mA)	Load Resistance (K?)	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
30	1000	1.5	5	7.5	3.1	2.2
30	1000	1.5	9	6.5	2.5	1.8
30	1000	1.5	7	6.6	2.6	1.8
30	1000	2	3	8.9	3.9	2.8
30	1000	2	4	8.0	3.4	2.4
30	1000	2	5	4.6	1.7	1.1
30	1000	2	7	6.4	2.5	1.7
30	1000	2	9	7.1	2.9	2.0
30	1000	3.5	3	4.1	1.4	1.0
30	1000	3.5	4	3.5	1.2	0.8
30	1000	3.5	5	2.8	0.9	0.6
30	1000	3.5	7	1.7	0.6	0.4
30	1000	3.5	9	1.9	0.6	0.4

Either the physician or the patient through magnet activation also can verify operation of Pulse Generators when output current is programmed to a level sufficient to cause strong tingling and/or hoarseness. Failure to detect stimulation after activation with a magnet may indicate EOS or high Lead impedance. If this occurs, the physician should try to reset the Pulse Generator following instructions in the Programming Wand Physician's Manual. If the Pulse Generator cannot be reset, replacement is indicated.

Cyberonics recommends daily magnet activation by the patient as the primary test for battery depletion due to the wide variation in the time (which can sometimes be very short) from the elective replacement indicator to the end of service.

⚠ Cyberonics recommends prompt replacement of the Pulse Generator at the end of battery life. Prompt replacement may help minimize any possible relapse in seizure control.

⚠ A Pulse Generator explanted for any reason should not be reimplanted. An explanted Pulse Generator should be returned to Cyberonics in a double-sealed pouch or container for examination and disposal, accompanied by a completed Returned Product Report. Before returning the Pulse Generator, disinfect the device components with Betadine®, Cidex® soak, or other similar disinfectant, and double-seal them in a pouch or other container properly labeled with a biohazard warning.

12.2 Physician Training/Information

Prescribing physicians are strongly encouraged to contact Cyberonics and request a referral to a physician experienced in the operational characteristics and functioning of the VNS Therapy System before prescribing use of the device for the first time. All VNS Therapy System programming should be by or under the supervision of a physician familiar in the use and operation of the Software.

Initial treatment output current (starting new or after Pulse Generator replacement) should be set at the lowest setting (0.25 mA). Subsequent and all future device settings should be made in 0.25 mA increments up to the desired treatment level (see the “Individualization of Treatment” section of this manual).

Physicians implanting the VNS Therapy System should be thoroughly familiar with all associated training materials, including the following:

- Product labeling for the Pulse Generator, Lead, and accessories, including Physician and Patient Manuals and Directions for Use
- “Implant Guide for the VNS Therapy System” training manual and other brochures
- Videotape on the proper implantation technique: “Implantation of the VNS Therapy System”
- Electrode practice fixture—a device used to practice placing the Lead coil around the left vagus nerve

In the event intolerable adverse events are reported, physicians should always try reducing the output current (mA) as a means of eliminating or reducing the severity of an event. Additionally, physicians should instruct patients or care givers on the application of the magnet to turn the Pulse Generator off (output current 0 mA) if an adverse event becomes intolerable.

12.3 Mechanism of Action

The precise mechanism(s) by which the VNS Therapy System exerts its anticonvulsant action is unknown. In animal models designed to examine anticonvulsant activity, vagus nerve stimulation prevented seizures or seizure spread in these models: maximum electroshock (MES), pentylenetetrazol (PTZ) tests, 3-mercaptopropionic acid (3-MPA), alumina gel, potassium penicillin, strychnine, and kindling. With the exception of the alumina gel model, vagus nerve stimulation did affect the heart and respiratory rate, which may have contributed to the alteration in seizure activity.

Localization of vagus-initiated activity in the brain has been observed through animal studies of *fos*[4] immunoreactivity, regional brain glucose metabolism, and positron emission tomography (PET) imaging in human patients.

4 *Fos* is a nuclear protein that is expressed under conditions of high neuronal activity.

An [^{15}O] H_2O PET study in 10 patients demonstrated that vagus nerve stimulation by the VNS Therapy System does increase blood flow in the rostral medulla, right thalamus, and right anterior parietal cortex, and bilaterally in the hypothalamus, anterior insula, and inferior cerebellum. Decreases in blood flow were detected bilaterally in the hippocampus, amygdala, and posterior cingulate gyrus.

12.4 Detailed Device Description

12.4.1. Physical Characteristics

The titanium case of the Pulse Generator is hermetically sealed and leak rate tested. Specially designed feedthroughs utilizing platinum conductors make the electrical connection from the connector blocks to the circuitry through the hermetically sealed enclosure.

Materials exposed to the subcutaneous environment are biologically compatible. All of these materials have a long history in medical implants and have been found to be tissue compatible in the vast majority of cases.

12.4.2. Power Source

The power source for the Model 102 and Model 102R Pulse Generator is a Wilson Greatbatch Ltd., Model 2075, lithium carbon monofluoride battery with an open-circuit voltage of 3.3. The battery's maximum available capacity is approximately 1.7 ampere-hours. The self-discharge reduces the capacity by less than 1 percent per year. This battery has a gradual drop in voltage near its end of life.

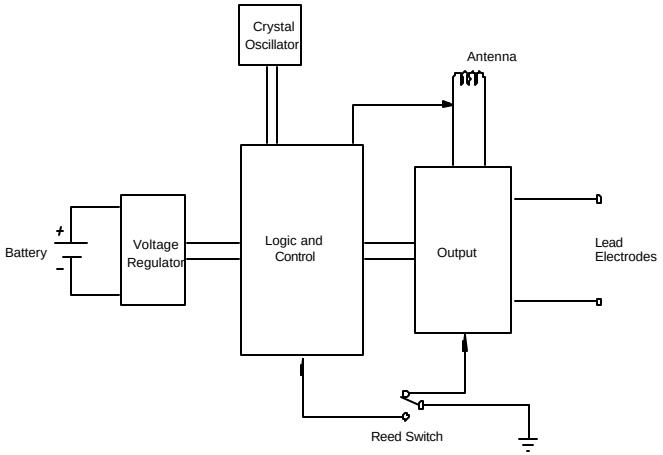
12.4.3 Circuitry

The Pulse Generator utilizes several complementary metal oxide semiconductor (CMOS) integrated circuits, including a microprocessor. The circuitry is schematically represented in Figure 15.

For descriptive purposes, circuitry of the Pulse Generator can be divided into the following major functional sections:

Voltage regulator	Regulates the system power supply.
Crystal oscillator	Provides a timing reference.
Logic and control	Controls overall Pulse Generator function; receives and implements programming commands; collects and stores telemetry information.
Output	Develops and modulates signals delivered to the Lead.
Antenna	Receives programming signals; transmits telemetry information to the Programming Wand.
Reed switch	Provides a mechanism to place the Pulse Generator in Magnet Mode or to inhibit its output.

Figure 15. Pulse Generator Circuitry

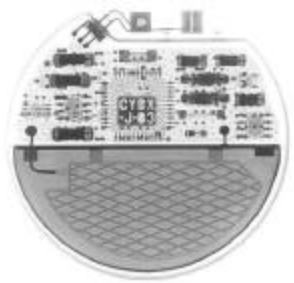


12.4.4 Identification

The Pulse Generator can be identified by x-ray and will appear as shown in Figure 16. The serial number and model number of the Pulse Generator are marked on its titanium case but do not appear on the x-ray. The serial number and model number can be identified by interrogating the Pulse Generator with the Model 250 Software and viewing the Device History screen (see the Model 250 Software Physician's Manual for details).

Figure 16. X-ray Identification

Model 102



The x-rays shown in Figure 16 show a Model 102 and a Model 102R. The x-ray tag included uses the following code:

CYBX-J-xx

where:

CYBX = Cyberonics

J = Model 102R or Model 102

Note: Serial numbers ? 1000000 = Model 102R
Serial numbers ? 1000000 = Model 102

xx = Year; e.g., 03 = 2003 (The Model 102 x-ray shown indicates that Cyberonics produced (initiation of final product assembly) this model in 2003.)

13. CYBERONICS' LIMITED REPLACEMENT WARRANTY

Cyberonics, Inc. warrants the VNS Therapy Pulse Generator against any defects due to faulty material or workmanship for a period of two years from the date of implantation. This warranty applies only to the original purchaser of the VNS Therapy Pulse Generator and the patient implanted with it. This Limited Replacement Warranty also applies only when the product is used in accordance with the product's Physician's Manual and excludes damage due to improper handling, defacing, accident (including dropping), or misuse. This product is not warranted when used or implanted by a person(s) not trained in or familiar with the VNS Therapy Lead, Pulse Generator, and Model 250 Software Physician's Manuals. This Limited Replacement Warranty is not a representation that any one VNS Therapy Pulse Generator will last the entire time of the Limited Replacement Warranty.

In no event shall Cyberonics, Inc. be liable for any special, incidental, indirect, or consequential damages based on the failure of the device to function within normal tolerances, or resulting from damage to the device by external forces, whether the claim is based on warranty, contract, tort, or otherwise, or in connection with the purchase, use, or surgical implantation of this device or associated components or costs over and above the original purchase price from Cyberonics, Inc.

To qualify for the Limited Replacement Warranty, the following conditions must be met:

1. A properly completed Implant and Warranty Registration Card for both the VNS Therapy Pulse Generator and the VNS Therapy Lead must be returned to Cyberonics, Inc. within sixty (60) days of device implantation;
2. The battery cannot have been depleted as a result of programming to unusually high output currents, pulse widths, or duty cycles, which will cause a high energy/current drain;
3. The product must have been used and prescribed in accordance with the VNS Therapy Lead, VNS Therapy Pulse Generator, and Model 250 Software Physician's Manuals;
4. The VNS Therapy Pulse Generator must have been implanted prior to its "Expiration Date";
5. The defective VNS Therapy Pulse Generator must be returned to Cyberonics, Inc. with an accompanying Return Goods Authorization (RGA) number, available from Technical Support at (800) 332-1375, and confirmed defective by the Quality Assurance Department; and
6. All returned VNS Therapy Pulse Generators shall become the property of Cyberonics, Inc.

If the VNS Therapy Pulse Generator becomes defective within the warranty period, contact Cyberonics, Inc. Customer Service for a no-cost replacement. Cyberonics, Inc. reserves the right to replace a defective product with the most comparable product currently available. Returned biohazardous product should be clearly identified as such on the outside surface of the package.

No implied warranty, including but not limited to, any implied warranty of merchantability or fitness for a particular purpose, shall extend beyond the period specified above. This replacement warranty shall be the exclusive remedy available to any person. No person has any authority to bind Cyberonics, Inc. to any representation, condition, or warranty except this Limited Replacement Warranty.

While this warranty gives you specific legal rights, you may also have other rights that vary from state to state or that encroach upon the above.

14. TROUBLESHOOTING

This section provides troubleshooting instructions in two parts: (1) in the Operating Room (OR) and (2) at patient follow-up visits.

14.1. Troubleshooting in the OR

14.1.1. Communication Problems in OR

A communication problem is a situation in which the Generator and Wand cannot clearly communicate with each other to interrogate, program, or run diagnostic tests. Communication problems can be caused by the following situations:

- a Programming Wand battery that may need to be replaced
- an interruption of a diagnostic test by prematurely moving the Programming Wand away from the Pulse Generator
- an electromagnetic interference (EMI)
- a Pulse Generator that could be at its end of service (EOS)
- a defective Programming Wand
- a defective Programming Computer
- a defective Pulse Generator

Communication problems are often intermittent and are rarely Pulse Generator related. These problems are normally due to the surrounding environment.

A communication problem causes an error message such as “data transmission error between programmer and device” during interrogation, when programming parameters or implant date/patient code, or when receiving “FAULT FAULT” results on a diagnostic test. To resolve the situation, perform the following steps:

1. Verify that the Programming Wand is properly connected to the Programming Computer (see Programming Wand Physician’s Manual for details).

2. Test the Programming Wand battery (see the following instructions for each model):

   Model 200:

   Using the tip of a ball-point pen or other similar object, press the RESET button, and then verify that the green POWER light comes on and stays on for approximately 25 seconds after the button is released. If it does not, the batteries should be replaced with brand new batteries. The Programming Wand uses two standard 9-volt alkaline batteries, which are located on the back of the Wand.

   Model 201:

   Briefly press the two red RESET buttons simultaneously, and then verify that the green POWER light comes on and stays on for approximately 25 seconds after the buttons are released. If it does not, the battery should be replaced with a brand new battery. The Programming Wand uses one standard 9-volt alkaline battery, which is located in the handle of the Wand.

3. Verify the proper positioning of the Programming Wand over the Pulse Generator. Reposition the Programming Wand by rotating the handle 45 degrees in either direction (see Physician's Manual for the Programming Wand for detail).
4. Extend the Programming Wand cable and ensure that the Wand is 3 to 4 feet away from the Programming Computer.
5. If communication is working while the Pulse Generator is outside the chest pocket and not inside the pocket, verify that the depth of the pocket is not greater than 1 inch or is not below muscle.
6. Verify that the Programming Computer is being run by its battery and is not plugged into a wall outlet.
7. Verify that the programming problem is not a result of electromagnetic interference (EMI) or noise from nearby electrical or magnetic equipment. Examples of possible sources of EMI are computer displays, portable telephones, fluorescent lighting, OR lights, and magnetic pads for surgical instruments. To check for EMI, perform the following steps:
    a. Press the RESET button(s) on the Programming Wand. (The green POWER light should come on and must stay on during EMI detection.)
    b. Move the Programming Wand closer to the suspected equipment (computer screen, OR lights, etc.)

- ? ? If EMI is detected, the yellow DATA/RCVD light will come on and remain on while in the presence of EMI.
- ? ? Programming, interrogating, or completing diagnostic tests in an area with EMI will be difficult or impossible. The problem can usually be resolved by repositioning the patient, the Programming Wand, or the EMI source.

8. Return to the Main Menu, and then turn off the Programming Computer.
9. Turn the Programming Computer back on and interrogate the device.

   Note: Cyberonics recommends interrogating the Pulse Generator as the last step of any programming session to verify correct settings for each parameter.

10. If problems persist, please contact Cyberonics at (800) 332-1375, ext. 7330.

14.1.2. High Lead Impedance on Lead Test in OR – Initial Implant

High Lead impedance in the OR can be caused by the following situations:

- ? ? incorrect placement of the Lead on the nerve
- ? ? incorrect connection of the Pulse Generator and Lead
- ? ? lack of irrigation of the vagus nerve
- ? ? a defective Lead
- ? ? a defective Pulse Generator

To resolve the situation, perform the following steps:

1. Verify that the Lead electrode(s) has been correctly placed on the vagus nerve.
2. Verify that the connector pin(s) is fully inserted into the Lead receptacle(s) in the Pulse Generator as follows:
    a. Tighten the setscrew(s) until the hex screwdriver begins to click.

       The pin(s) should be visible in the area at the back end of the connector block.
    b. Gently pull on the connector boot(s) to verify that the pin(s) is securely tightened.
3. Verify the vagus nerve is adequately irrigated.
4. Re-run the Lead Test.
5. If “HIGH” Lead impedance is still noted, perform a Pre-implant Test as follows:
    a. Remove the Lead connector pin(s) from the Lead receptacles.
    b. Insert the connector pin(s) of the test resistor assembly into the Lead receptacle(s) in the Pulse Generator header.
    c. Tighten the setscrew(s) until the hex screwdriver begins to click.

6.

IF…	THEN…
The Pre-implant Test indicates “HIGH” Lead impedance	1. Do not implant the Pulse Generator. 2. Please Call Cyberonics at (800) 332-1375, ext. 7330.
The Pre-implant Test indicates “OK” Lead impedance	1. Remove the test resistor. 2. Re-insert the Lead connector pin(s). 3. Properly tighten the setscrew(s) until the hex screwdriver begins to click. 4. Continue to the next step.

7. Perform the Lead Test.

8. If the Lead Test continues to indicate “HIGH” Lead impedance, do not implant the Lead and please contact Cyberonics at (800) 332-1375, ext. 7330.

14.1.3. High Lead Impedance on Lead Test in OR – Generator Replacement

High Lead impedance in the OR can be caused by the following situations:

- ? ? incorrect connection of the Pulse Generator and Lead
- ? ? a defective Lead
- ? ? a defective Pulse Generator

To resolve the situation, perform the following steps:

1. Verify that the connector pin(s) is fully inserted into the Lead receptacle(s) in the replacement Pulse Generator as follows:
   a. Tighten the setscrew(s) until the hex screwdriver begins to click.
      The pin(s) should be visible in the area at the back end of the connector block.
   b. Gently pull on the connector boot(s) to verify that the pin(s) is securely tightened.
2. Re-run the Lead Test.
3. If “HIGH” Lead impedance is still noted, perform a Pre-implant Test as follows.
   a. Remove the Lead connector pin(s) from the Lead receptacle(s).
   b. Insert the connector pin(s) of the test resistor assembly into the Lead receptacle(s) in the Pulse Generator header.
   c. Tighten the setscrew(s) until the hex screwdriver begins to click.

4.

IF …	THEN…
The Pre-implant test indicates “HIGH” Lead impedance	1. Do not implant the Pulse Generator. 2. Please Call Cyberonics at (800) 332-1375, ext. 7330.
The Pre-implant test indicates “OK” Lead impedance	1. Remove the test resistor. 2. Re-insert the Lead connector pin(s). 3. Properly tighten the setscrew(s) until the hex screwdriver begins to click. 4. Continue to the next step.

5. Perform the Lead Test.
6. If the Lead Test continues to indicate “HIGH” Lead impedance, the Lead needs to be replaced. Please contact Cyberonics at (800) 332-1375, ext. 7330.

14.2. Troubleshooting at Follow-Up Visits

14.2.1. Communication Problems at Follow-Up Visits

A communication problem is a situation in which the Generator and Wand cannot clearly communicate with each other to interrogate, program, or run diagnostic tests. Communication problems can be caused by either of the following situations:

- a Programming Wand battery that may need to be replaced
- an interruption of a diagnostic test by prematurely moving the Programming Wand away from the Pulse Generator
- an electromagnetic interference (EMI)
- a Pulse Generator that could be at its end of service (EOS)
- a defective Programming Wand
- a defective Programming Computer
- a defective Pulse Generator

Communication problems are often intermittent and are rarely Pulse Generator related. They are normally due to the surrounding environment.

A communication problem causes an error message such as “data transmission error between programmer and device” during interrogation, when programming parameters or implant date/patient code, or when receiving “FAULT FAULT” results on a diagnostic test. To resolve the situation, perform the following steps:

1. Verify that the Programming Wand is properly connected to the Programming Computer (see Programming Wand Physician’s Manual for details).
2. Test the Programming Wand battery (see the following instructions for each model).

Model 200:

Using the tip of a ball-point pen or other similar object, press the RESET button, and then verify that the green POWER light comes on and stays on for approximately 25 seconds after the button is released. If it does not, the batteries should be replaced with brand new batteries. The Programming Wand uses two standard 9-volt alkaline batteries, which are located on the back of the Wand.

Model 201:

Briefly press the two red RESET buttons simultaneously, and then verify that the green POWER light comes on and stays on for approximately 25 seconds after the buttons are released. If it does not, the battery should be replaced with a brand new battery. The Programming Wand uses one standard 9-volt alkaline battery, which is located in the handle of the Wand.

3. Verify the proper positioning of the Programming Wand over the Pulse Generator. Reposition the Programming Wand by rotating the handle 45 degrees in either direction (for detail, see the Programming Wand Physician's Manual).
4. Extend the Programming Wand cable and ensure that the Wand is 3 to 4 feet away from the Programming Computer.
5. Verify that the Programming Computer is being run by its battery and is not plugged into a wall outlet.

6. Verify that the programming problem is not a result of electromagnetic interference (EMI) or noise from nearby electrical or magnetic equipment. Examples of possible sources of EMI are computer displays, portable telephones, and fluorescent lighting. To check for EMI, perform the following steps:
   a. Press the RESET button(s) on the Programming Wand. (The green POWER light should come on and must stay on during EMI detection.)
   b. Move the Programming Wand closer to the suspected equipment (computer screen, fluorescent lighting, etc.)
      ? ? If EMI is detected, the yellow DATA/RCVD light will come on and remain on while in the presence of EMI.
      ? ? Programming, interrogating, or completing diagnostic tests in an area with EMI will be difficult or impossible. The problem can usually be resolved by repositioning the patient, the Programming Wand, or the EMI source.
7. Return to the Main Menu, and then turn off the Programming Computer.
8. Turn the Programming Computer back on and interrogate the device.

   Note: Cyberonics recommends interrogating the Pulse Generator as the last step of any programming session to verify correct settings for each parameter.
9. If problems persist, please contact Cyberonics at (800) 332-1375, ext. 7330.

14.2.2. High Lead Impedance on a Diagnostic Test at Follow-Up Visit

High Lead impedance at a follow-up visit can be caused by either of the following situations:

- ? ? Fibrosis between the nerve and the electrode
- ? ? Lead fracture
- ? ? Lead disconnection from the Pulse Generator
- ? ? High battery impedance approaching end of service (EOS).

To resolve the situation, perform the following steps:

1. Interrogate the device.
2. Perform a Lead Test and record all the results.

   ⚠ For the Lead Test, the Software automatically programs the Pulse Generator to 1.0 mA, 500 ?sec, and 20 Hz. Patients whose Pulse Generator output current is normally *less* than these values may experience increased sensation, coughing, a flushed face, or other effects. See the Adverse Events section in this manual for a complete list of possible adverse events.
3. Perform a Normal Mode Diagnostics Test and record all the results.

   Note: To obtain accurate information from the device diagnostics, the Pulse Generator must be programmed to a **minimum** of .75 mA, 15 Hz, and **at least** 30 seconds ON time.
4. Refer to the following table to determine the possible cause of the “HIGH” Lead impedance result.

IF…	THEN…
Lead Test Results = DC-DC code: 7 Output Current: LIMIT Lead Impedance: HIGH **Normal Mode Results =** DC-DC code: 7 Output Current: LIMIT Lead Impedance: HIGH	**Possible Causes:** **ERI – Yes:** End of service is pending. Consider generator replacement. **ERI- No:** Possible fibrosis between the nerve and electrode, Lead fracture, Lead disconnection from the Pulse Generator, or high battery impedance approaching end of service
Lead Test Results = DC-DC code: 4-7 Output Current: OK Lead Impedance: HIGH **Normal Mode Results =** DC-DC code: 7 Output Current: LIMIT Lead Impedance: HIGH	**Possible Causes:** **ERI – Yes:** End of service is pending. Consider Generator replacement. **ERI- No:** Possible fibrosis between the nerve and electrode, or high battery impedance approaching end of service. Generator cannot deliver programmed output.

IF…	THEN…
Lead Test Results = DC-DC code: 0-3 Output Current: OK Lead Impedance: OK **Normal Mode Results =** DC-DC code: 7 Output Current: LIMIT Lead Impedance: HIGH	**Possible Causes:** **ERI – Yes:** End of service is pending. Consider Generator replacement. **ERI- No:** Generator cannot deliver programmed output. Consider reducing output current or frequency and widening pulse width.
Lead Test Results = DC-DC code: 0-3 Output Current: OK Lead Impedance: OK **Normal Mode Results =** DC-DC code: 0-6 Output Current: OK Lead Impedance: OK	**Possible Causes:** **ERI – Yes:** End of service is pending. Consider Generator replacement. **ERI- No:** Pulse Generator is delivering output as intended.

5. Please contact Cyberonics at (800) 332-1375, ext.7330 to report any incidences of high impedance.

14.2.3. “Patient Cannot Feel Stimulation” at Follow-Up Visit

A patient may not feel stimulation if either of the following situations exist:

- Patient has become accustomed to the programmed setting.
- Device is approaching its end of service (EOS).
- Lead discontinuity.
- Issue with the Pulse Generator.

To determine the cause of the situation, perform the following steps:

1. Swipe the magnet. Ask the patient if they feel the magnet activation, experience any voice alteration, or experience any other common side effect to indicate the presence of stimulation.

   Note: Ensure that the technique for swiping the magnet over the device is correct according to the section “Initiating Stimulation with a Magnet” in Chapter 12. Also, refer to the section“Potential Adverse Events” in Chapter 6 for a complete list of possible adverse events.

2. Interrogate the Pulse Generator.
3. Perform a Lead Test and record the results.

   If the results indicate “OK” Lead Impedance, the system is functioning properly and the patient could have become accustomed to the settings, as do many patients.

⚠ For the Lead Test, the Software automatically programs the Pulse Generator to 1.0 mA, 500 ?sec, and 20 Hz. Patients whose Pulse Generator output current is normally *less* than these values may experience increased sensation, coughing, a flushed face, or other effects. See the Adverse Events chapter in this manual for a complete list of possible adverse events.

4. Perform a Normal Mode Diagnostic Test and record the results.

IF…	THEN…
The Normal Mode Diagnostic Test indicates the Output Current is "LIMIT"	The Pulse Generator cannot deliver programmed output. Consider reducing output current or frequency and widening the pulse width.
The Normal Mode Diagnostic Test indicates the Output Current is "OK"	The Pulse Generator can deliver the programmed output current. **Note**: To obtain accurate information from the device diagnostics, the Pulse Generator must be programmed to a **minimum** of .75 mA, 15 Hz, and **at least** 30 seconds ON time.
The Normal Mode Diagnostic Test indicates "HIGH" Lead Impedance	Please see the previous Troubleshooting section, "High Lead Impedance on Diagnostic Test at Follow-Up Visit".

5. If further assistance is needed, please contact Cyberonics at (800) 332-1375, ext. 7330.

A patient's magnet activation may not be working if either of the following situations exists:

- ? ? An incorrect technique is used for swiping the magnet.
- ? ? Magnet output current is not programmed to ON.
- ? ? Device is approaching its end of service (EOS).
- ? ? Device was implanted too deep.
- ? ? Issue with the Pulse Generator.
- ? ? Patient may have become accustomed to the programmed setting.

To determine the cause of the situation, perform the following steps:

1. Interrogate the device.
2. Confirm that the Magnet Output Current is ?.25 mA and Magnet ON time is ?7 seconds.
3. Display the Device History screen and record the number of magnet activations listed on the screen.
4. Swipe the magnet over the device and watch for a clinical response to the stimulation. Wait 3 to 4 minutes and re-interrogate the device.

   Note: Ensure that the technique for swiping the magnet over the device is correct according to the section "Initiating Stimulation with a Magnet" in this manual.

5. Display the Device History screen and record the number of magnet activations listed on that screen. The number of activations should have increased by 1.

6. If the magnet activation shows up on the Magnet History screen but the patient does not feel magnet-induced stimulation, increase the magnet output current until the magnet-induced stimulation is felt.
7. If the number of magnet activations did not increase, go to the Device Diagnostics screen and perform a Magnet Mode Diagnostic test and record all results.

   Note: Follow the listed instructions and swipe the magnet just before starting the test. To obtain accurate information from the device diagnostics, the Pulse Generator magnet output must be programmed to a **minimum** of .75 mA, 15 Hz, and 30 seconds ON time.

IF…	THEN…
The Magnet Mode Diagnostic Test indicates device status "MAGNET MODE" and output current is "OK"	The magnet is functioning properly and the patient could have become accustomed to the settings, as do many patients.
The Magnet Mode Diagnostic Test indicates device status "STANDBY" and output current "****",	Perform steps 1 through 7 with an alternate Cyberonics magnet.
The Magnet Mode Diagnostic Test indicates "HIGH" Lead Impedance	Please see the previous Troubleshooting section "High Lead Impedance on Diagnostic Test at Follow-Up Visit.

8. If further assistance is needed, please contact Cyberonics at (800) 332-1375, ext. 7330.

15. INFORMATION AND SUPPORT

If there are questions regarding use of the VNS Therapy System or any of its accessories, please contact Cyberonics:

USA

Cyberonics, Inc.
100 Cyberonics Boulevard
Houston, Texas 77058

Telephone: (281) 228-7200
Fax: (281) 218-9332

For 24-hour support, please call:

Telephone: (800) 332-1375	General Operator
Ext 7330	Technical Support
Ext 7337	Clinical Support

Europe

Cyberonics Europe, S.A.
Belgicastraat 9
1930 Zaventem
Belgium

Telephone: 32 2 720 95 93
Fax: 32 2 720 60 53

Internet

www.cyberonics.com

16. GLOSSARY

ACLS	Advanced Cardiac Life Support
AE	Adverse event.
AED	Antiepileptic drug(s).
BOL	Beginning of Life
Duty cycle	Percentage of time during which stimulation occurs; stimulation time (programmed ON time plus two seconds of ramp-up time and two seconds of ramp-down time) divided by the sum of signal ON and OFF times.
EAS	Electronic article surveillance
EMI	Electromagnetic interference.
EOS	End of service
ERI	Elective replacement indicator
Excess duty cycle	Duty cycle for which the ON time is greater than the OFF time.
Generalized onset seizure	Type of seizure that involves all parts of the brain and, usually, an alteration in consciousness.
High Lead impedance	DC-DC Converter Codes greater than four on a device diagnostic test; not a sole determinant of a need for Lead replacement.
LIMIT output current	Output current other than that which was programmed; not a sole indicator of a device malfunction.

Magnet activation	Brief magnet application and removal, which initiates a stimulation.
Microcoulomb	Product of current and time, or output current (in mA) multiplied by the pulse width (in msec).
Nominal parameters	Specific preset parameters available with the software; Cyberonics suggests that the Pulse Generator be set to these parameters when patients are first stimulated (see the "Specifications and Product Information" section for specific nominal parameters).
Output current	Amount of electrical current delivered in a single pulse of a stimulation, measured in mA.
Patient code	Any three-digit combination assigned by the treating physician; generally programmed at time of implantation; often patient's initials: first, middle, last (or with a hyphen for no known middle initial).
Partial onset seizure	Type of seizure that begins focally with a specific sensory, motor, or psychic aberration that reflects the affected part of the cerebral hemisphere where the seizure originated.
Pulse width	Duration of a single pulse within a stimulation, measured in ?sec.

Ramp-down	Gradual decrease over approximately two seconds in output current at the end of stimulation greater than 10 Hz in signal frequency.
Ramp-up	Gradual increase over approximately two seconds in output current at the beginning of stimulation greater than 10 Hz in signal frequency.
Refractory	Resistant to previous treatment alternatives defined by the treating physician; generally refers to the epilepsy of patients who have tried and failed two or more antiepileptic drugs.
Reset parameters	Parameters to which the Pulse Generator internally programs when it is reset (see the “Specifications and Product Information” section for specific reset parameters).
SAE	Serious adverse event.
Signal frequency	Repetition rate of pulses in a stimulation; measured in number of pulses per second (Hz).
Signal OFF time	Interval between stimulations when there is no stimulation; measured in minutes.
Signal ON time	Length of time the programmed output current is delivered (not including ramp-up and ramp-down times); measured in seconds.

Stimulation parameters	Programmed pulse width, output current, signal frequency, ramp-up time, ramp-down time, and signal ON time.
Stimulation time	Therapeutic output of the VNS Therapy Pulse Generator; consists of the signal ON time, plus two seconds of ramp-up time and two seconds of ramp-down time.
SUDEP	Sudden unexplained death in epilepsy.
Vagus nerve	Either of the pair of tenth cranial nerves arising from the medulla and supplying mainly the viscera, especially with autonomic sensory and motor fibers; in this document, *vagus nerve* always refers to the *left* vagus nerve.
VNS™	Vagus nerve stimulation.